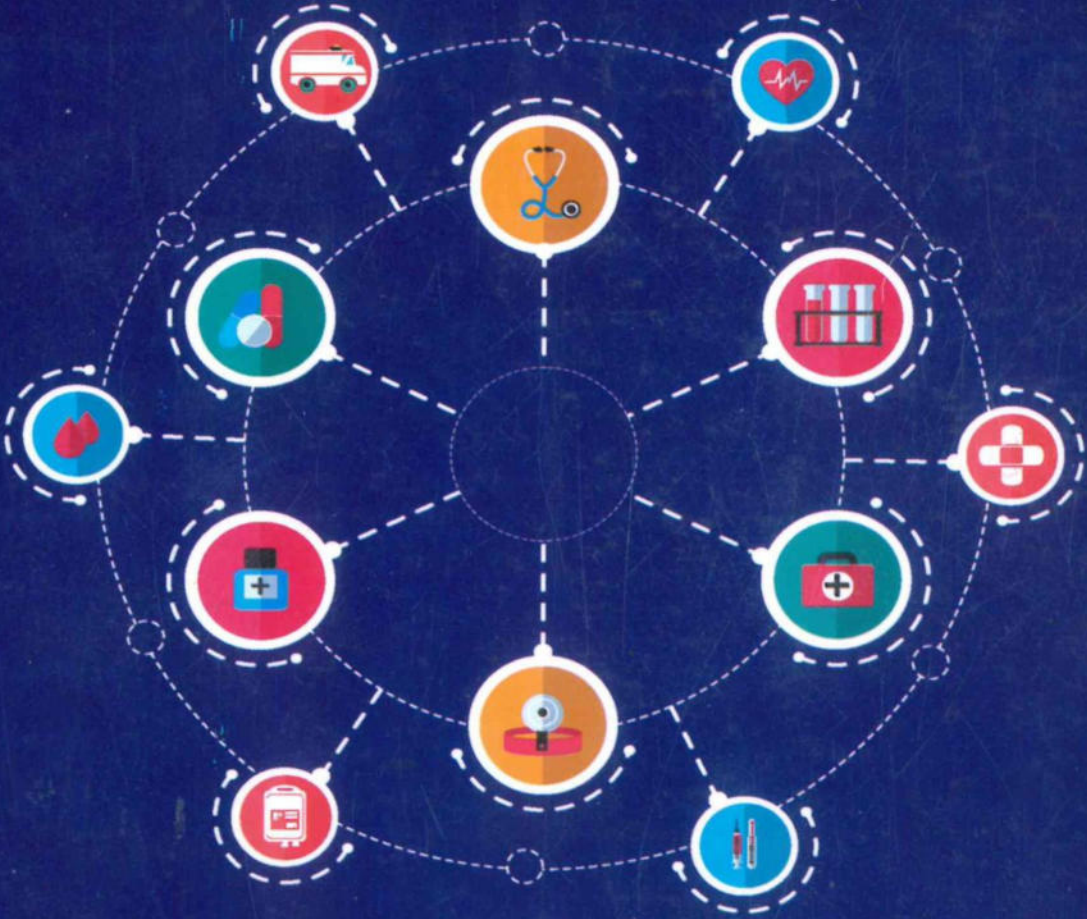
Clinical Decision in
Critical Care

Third Edition

Part 2



Ahmed Mukhtar, MD

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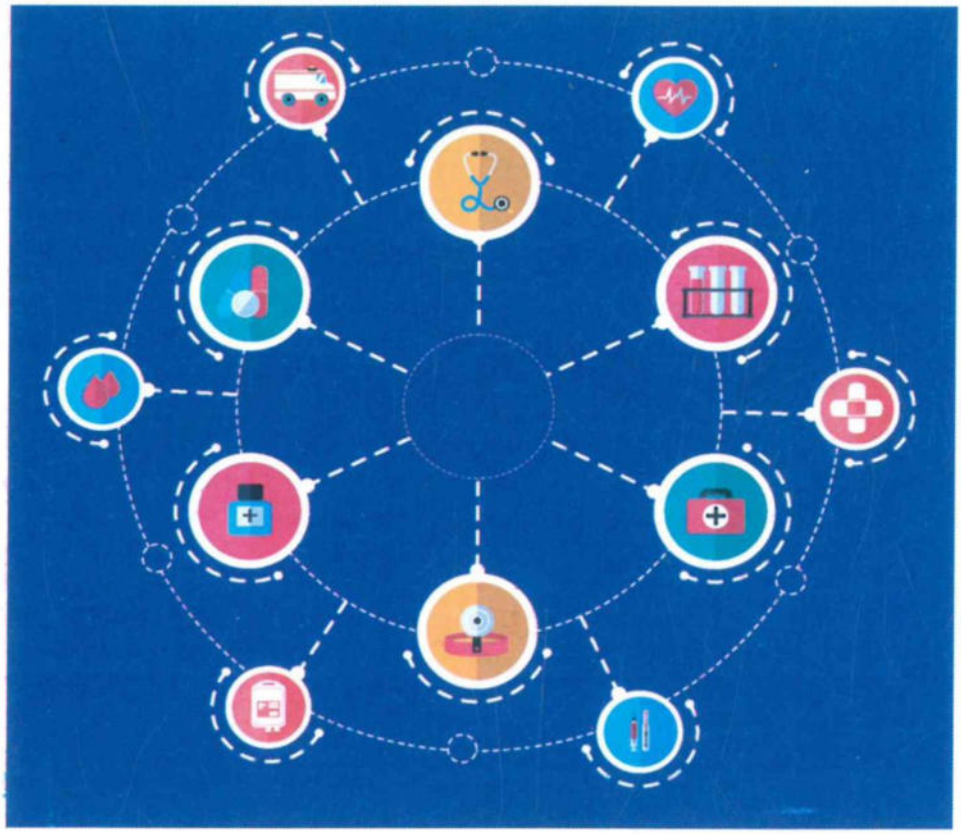

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SECTION 8

Thromboprophylaxis, venous thromboembolism, and anticoagulation

Chapter 37

Prophylaxis of venous thromboembolism

General Principles

- Critically ill patients are heterogenous group of population which include critically ill non-surgical patients, surgical non-orthopedic patients, surgical orthopedic patients, trauma patients, and pediatric patients
- The risk of venous thromboembolism (VTE) should be balanced against the bleeding risk
- The risk of thromboembolism can be assessed by Padua prediction score in medically ill patients and by Caprini score in surgical patients
- Padua score ≥ 4 points and Caprini score ≥ 5 indicates high risk of VTE
- D-Dimers alone at a level higher than 2-times the upper normal limit of the assay leads to identification of patients at high VTE risk
- IMPROVE Bleed score has been recently validated for evaluation of bleeding risk. IMPROVE bleed score ≥ 7 indicate high bleeding risk
- Pharmacologic methods are the preferred methods against DVT prophylaxis when thromboembolic risk is high and bleeding risk is low
- Mechanical methods of prophylaxis (intermittent pneumatic compression IPC) should be used routinely in whom pharmacological prophylaxis is contraindicated because of high bleeding risk.

Scoring system to evaluate risk of thrombosis and risk of bleeding

- Padua risk assessment model should be used to assess VTE risk in medical patients.
  - » Padua prediction Score ≥ 4 indicates high risk of VTE
- Caprini risk assessment model should be used to assess VTE risk in surgical patients
  - » Caprini Score ≥ 5 indicates high risk of VTE
- Bleeding score can be used to assess bleeding risk in critically ill patients
  - » Bleeding Score ≥ 7 indicates high risk of bleeding

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Table 37-1:Padua Prediction Score

Item	Score
Previous VTE	3
Reduced Mobility (bed rest with for at least 3 days)	3
Thrombophilic Condition (defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, or antiphospholipid syndrome)	3
Active Cancer (local or distant metastases and with chemotherapy or radiation in the previous 6 months)	3
Recent (< 1month) Trauma/Surgery	2
Age ≥ 70 years	1
Heart or Respiratory Failure	1
Acute Myocardial Infarction or Ischemic Stroke	1
Acute Infection or Rheumatologic Disorder	1
BMI ≥ 30	1

Table 37-2:Caprini Prediction Score

1 Point	2 Point	3 Point	4 Point
Age 41-60	Age 61-74	Age ≥ 75	Acute spinal cord injury (< 1 mo)
Acute MI (<1 mo)	Central venous access	Established thrombophilia	Elective lower extremity arthroplasty
BMI > 25	Immobile > 72 hrs	HIT	Stroke (< 1 mo)
CHF exacerbation (<1 mo)	Leg plaster cast or brace	Hx of VTE	
Hx of inflammatory bowel disease	Malignancy	Family hx VTE (1 degree relative)	
Procedure with local anesthesia	Surgery- arthroscopic		
Swollen legs or Varicose veins	Surgery > 45 mins		
Sepsis (< 1 mo)			
Serious lung dx ex. Pneumonia (<1 mo)			
1point (For Women Only)			
Oral contraceptives or HRT			
Pregnancy or postpartum (< 1 month)			
Hx of unexplained stillborn infant, spontaneous abortion (≥3), premature birth with toxemia or growth restricted infant			

Table 37-3:Bleeding Risk Score

Bleeding Risk Score	Points
Moderate renal failure (GFR 30-59)	1
Male vs female	1
Age >40-84	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
ICU/CCU	2.5
Severe renal failure, GFR < 30	2.5
Hepatic failure (INR > 1.5)	2.5
Age ≥ 85	3.5
Platelet count less than 50	4
Bleeding in the 3 months before admission	4
Active peptic ulcer	4.5

Protocol of VTE Prophylaxis in Critically ill Medical Patients

- Assess all patients on ICU admission for risk of thrombosis and risk of bleeding and subsequently daily.
- In patients with low risk of VTE (Padua score < 4) SHOULD NOT prophylaxis against VTE
- In patients with high risk of VTE (Padua score ≥ 4) should receive pharmacological prophylaxis
- In patients with high risk of VTE and with either active bleeding or at high risk of bleeding (bleeding score ≥ 7) should receive mechanical prophylaxis alone until the bleeding risk decrease
- Routine use of ultrasound to screen for DVT IS NOT recommended.

Table 37-4: Protocol of VTE prophylaxis in medical patients

Points	Risk	Recommendation
< 4	Low VTE Risk	VTE prophylaxis not needed
≥ 4	High VTE Risk and Low Bleed Risk (<7)	Pharmacologic Prophylaxis
≥ 4	High VTE Risk and High Bleed Risk (≥7)	Mechanical Prophylaxis

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Thromboprophylaxis in Special Population

- Severe renal insufficiency: the drugs of the choice for VTE prophylaxis in these patients are low dose unfractionated heparin, dalteparin, or reduced dose of LMWH
- Patients with liver cirrhosis:
  - Padua is used for risk stratification.
  - Patients with high risk of VTE and low risk of bleeding should receive LMWH
  - Patients with high risk of VTE and high risk of bleeding should receive mechanical prophylaxis
  - Bleeding risk increased in patients with
    - Recent bleeding
    - Platelet count < 50000
    - Untreated varices > grade 2
- Patients with acute ischemic stroke (AIS)
  - For immobile patients with high risk of VTE IPC is recommended for prevention of VTE
  - Graduated compression stocking (GCS) alone is not recommended for VTE prevention in patient with AIS.
  - The role of LMWH or UFH in prevention of VTE in AIS is not clear
- Patients with intracerebral hemorrhage
  - IPC should be used upon hospital admission
  - LMWH or UFH could be added after 48 hours If the hematoma is stable and no ongoing coagulopathy
  - IPC is preferred to be continued after starting pharmacological prophylaxis
- Patients with aneurysmal subarachnoid hemorrhage
  - IPC should be used upon hospital admission
  - VTE prophylaxis with UFH at least 24 h after an aneurysm has been secured by surgical approach or by coiling
- Patients with brain tumors
  - VTE prophylaxis with either LMWH or UFH upon hospitalization for patients with brain tumors who are at low risk for major bleeding

Protocol of VTE prophylaxis in critically ill surgical patients (Abdominal, Pelvic, Thoracic Surgery)

- Assess all patients on ICU admission for risk of thrombosis and risk of bleeding and subsequently daily.
- In patients with very low risk of VTE SHOULD NOT receive prophylaxis against VTE
- In patients with low risk of VTE (Caprini score, 1-2) should receive IPC
- In patients with moderate to moderate risk of VTE (Caprini score 3-4) with no active bleeding or at high risk of bleeding should receive either pharmacological or mechanical prophylaxis.
- In patients with moderate to high risk of VTE (Caprini score ≥ 5) with no active bleeding or at high risk of bleeding should receive either pharmacological or mechanical prophylaxis

- In patients with moderate to high risk of VTE and with either active bleeding or at high risk of bleeding (bleeding score ≥7) should receive mechanical prophylaxis alone until the bleeding risk decrease

Table 37-5:Protocol of VTE prophylaxis in surgical patients

Points	Risk	Recommendation
0	Very low VTE Risk	Early and frequent ambulation
1-2	Low VTE Risk	Mechanical Prophylaxis
3-4	Moderate VTE Risk and Low Bleed Risk	Pharmacologic Prophylaxis
≥ 5	High VTE Risk and Low Bleed Risk (<7)	Mechanical AND Pharmacologic Prophylaxis

Protocol of VTE Prophylaxis in Orthopedic Patients

- In patients undergoing total hip arthroplasty (THA), total knee arthroplasty (TKA), or hip fracture surgery (HFS) should receive one of the following agents
    - » LMWH or UFH
    - » Fondaparinux
    - » Warfarin
    - » New oral anticoagulant
    - » Aspirin
- Recent European guidelines suggest use of aspirin alone instead of other phramacologic agents for VTE prevention in THA, TKA, and HFS.

Table 37-6:Options of VTE in patients undergoing THA, TKA, and HFS

Agent	Cr Cl ≥ 30 ml/min	Cr Cl < 30 ml/min
Enoxaparin	40 mg SC /24 hrs	30 mg SC q 24 hrs
Rivaroxaban	10 mg oral once daily	Avoid use
Apixaban	2.5 mg oral twice daily	Avoid use in Cr Cl < 15 ml/min
Fondaparinux	2.5 mg SC /24 hrs	Avoid use
Warfarin	Target INR 1.8-2.2	Target INR goal 1.8-2.2
Aspirin	81 mg oral once daily	81 mg oral once daily

Protocol of VTE prophylaxis in trauma patients

- All patients receive IPC as soon as possible after the second survey (excluding anatomical constraints).
- If patients have an immediate surgery or interventional radiology procedure, the intermittent pneumatic compression devices are set up post-operatively
- Pharmacological prophylaxis by LMWH or UFH should be started after 6 h post-operatively or following any invasive procedure in the absence of brain injury or latent hemorrhagic risk
- For patients in hemorrhagic shock, heparin is started after bleeding control and restoration of biological hemostasis (platelets > 80.000/mm3, prothrombin time > 40%)
- For patients having a latent hemorrhagic risk (large solid organ contusion without

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embolization procedure, communitive pelvic fracture, refractory epistaxis, etc.), the chemical prophylaxis is started after the first 24 h

- Traumatic brain injury (TBI) and spinal cord injury
  - IPC within 24 hours of TBI should be initiated
  - LMWH or UFH 48 hours should be initiated after injury or neurosurgical intervention when a head CT scan shows stability of brain injuries

Duration of thromboprophylaxis

- For moderate risk patients undergoing major general and abdominal-pelvic surgical procedures, thromboprophylaxis should be continued until hospital discharge
- For those who have undergone major cancer surgery or have previously had VTE, thromboprophylaxis should be continued for up to 28 days
- For patients undergoing total hip replacement or hip fracture surgery, thromboprophylaxis should be extended beyond 10 days and up to 35 days after surgery.

Table 37-7:Agents used for VTE pharmacologic prophylaxis

	Cr Cl ≥ 30 ml/min	Cr Cl < 30 ml/min	Weight > 100 kg and/or BMI > 40 with Cr Cl ≥ 30 ml/min	Weight > 100 kg and/or BMI > 40 wither Cl < 30 ml/min	Weight < 50 kg with Cr Cl ≥ 30 ml/min
Enoxaparin	40 mg SC once daily	30 mg SC once daily	40 mg SC every 12 hrs	Not recommended	40 mg/24 hrs
Tinzaparin* Innohep®	Orthopedic: SC 75 unit/kg (actual body weight) once daily General surgery: SC 3500 unit once daily (BMI ≥ 40Kg/m2)	Not recommended	4500 once daily		
Recombinant Hirudin Rb variant Thrombex	Cr Cl > 60 ml/min SC :15mg Q12 hrs CrCl 31-60 ml/min : 5mg Q12 (33 IU by insulin syringe)	CrCl ≤ 30ml/min: 1.7mg Q12 (11 IU by insulin syringe)			
Fondaparinux	2.5 mg SC once daily	Contraindicated	2.5 mg SC once	Contraindicated	Not recommended
Heparin	5000 units SC BID orTDS	5000 units SC BID orTDS	7500 units TDS	7500 units TDS	5000 units SC BID orTDS
New oral anticoagulant (in orthopedic surgery)	NOAC are not recommended in patients with Cr Cl < 30 ml/min Dabigatran (Pradaxa): 110 mg for the first day, then 220 mg once daily Apixaban (Eliquis): 2.5 mg twice daily. Rivaroxaban (Xarelto): 10 mg once daily, with or without food.				

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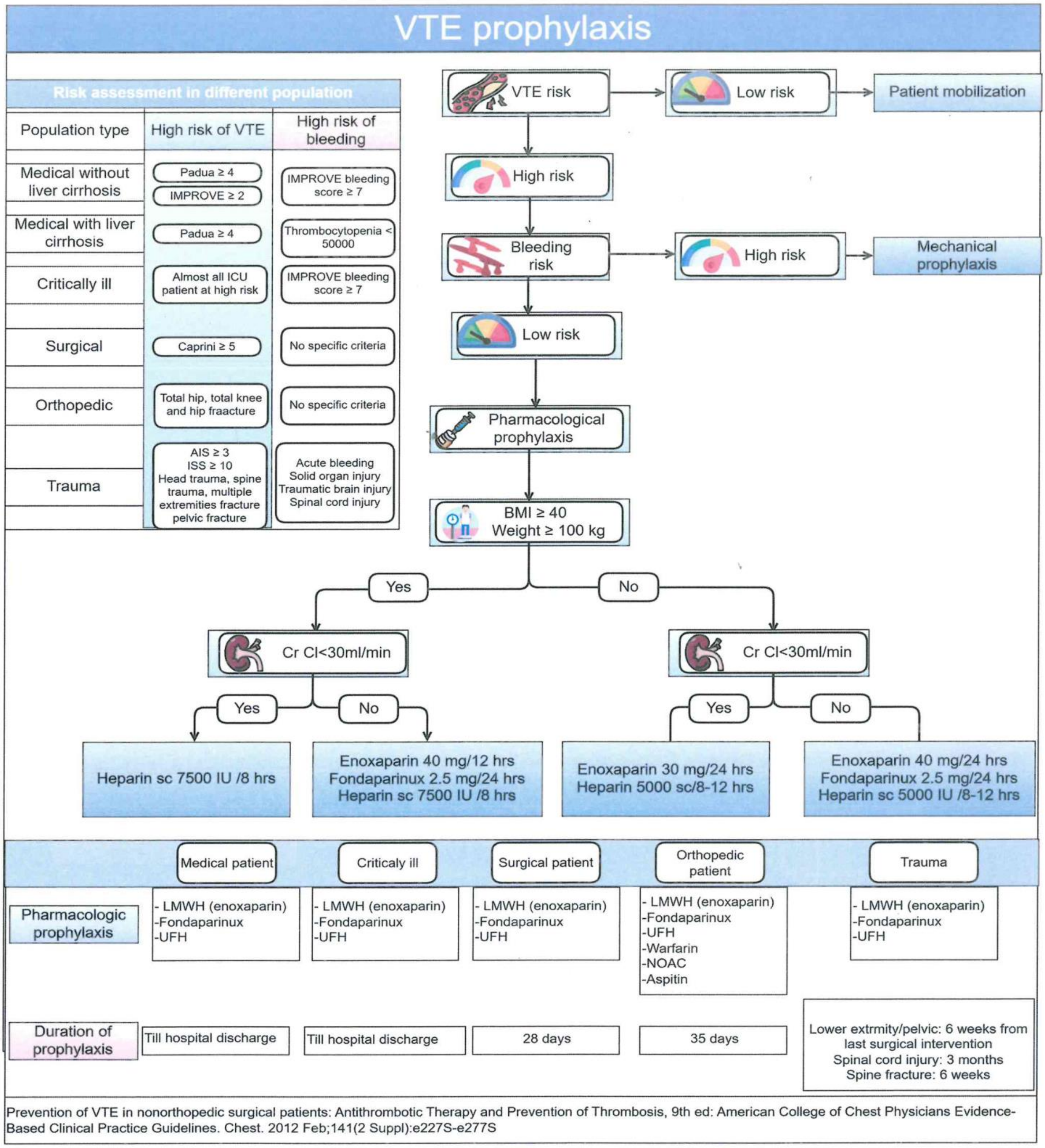

VTE prophylaxis

Risk assessment in different population

Population type	High risk of VTE	High risk of bleeding
Medical without liver cirrhosis	Padua ≥ 4 IMPROVE ≥ 2	IMPROVE bleeding score ≥ 7
Medical with liver cirrhosis	Padua ≥ 4	Thrombocytopenia < 50000
Critically ill	Almost all ICU patient at high risk	IMPROVE bleeding score ≥ 7
Surgical	Caprini ≥ 5	No specific criteria
Orthopedic	Total hip, total knee and hip fraacture	No specific criteria
Trauma	AIS ≥ 3 ISS ≥ 10 Head trauma, spine trauma, multiple extremities fracture pelvic fracture	Acute bleeding Solid organ injury Traumatic brain injury Spinal cord injury

VTE risk
Low risk
Patient mobilization
High risk
Bleeding risk
High risk
Mechanical prophylaxis
Low risk
Pharmacological prophylaxis
BMI ≥ 40
Weight ≥ 100 kg
Yes
No
Cr Cl<30ml/min
Cr Cl<30ml/min
Yes
No
Yes
No
Heparin sc 7500 IU /8 hrs
Enoxaparin 40 mg/12 hrs
Fondaparinux 2.5 mg/24 hrs
Heparin sc 7500 IU /8 hrs
Enoxaparin 30 mg/24 hrs
Heparin 5000 sc/8-12 hrs
Enoxaparin 40 mg/24 hrs
Fondaparinux 2.5 mg/24 hrs
Heparin sc 5000 IU /8-12 hrs

	Medical patient	Criticaly ill	Surgical patient	Orthopedic patient	Trauma
Pharmacologic prophylaxis	- LMWH (enoxaparin) -Fondaparinux -UFH	- LMWH (enoxaparin) -Fondaparinux -UFH	- LMWH (enoxaparin) -Fondaparinux -UFH	- LMWH (enoxaparin) -Fondaparinux -UFH -Warfarin -NOAC -Aspitin	- LMWH (enoxaparin) -Fondaparinux -UFH
Duration of prophylaxis	Till hospital discharge	Till hospital discharge	28 days	35 days	Lower extrmity/pelvic: 6 weeks from last surgical intervention Spinal cord injury: 3 months Spine fracture: 6 weeks

Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e227S-e277S

Figure 37-1:Algorithm of VTE prophylaxis in critically ill patients

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Chapter 38

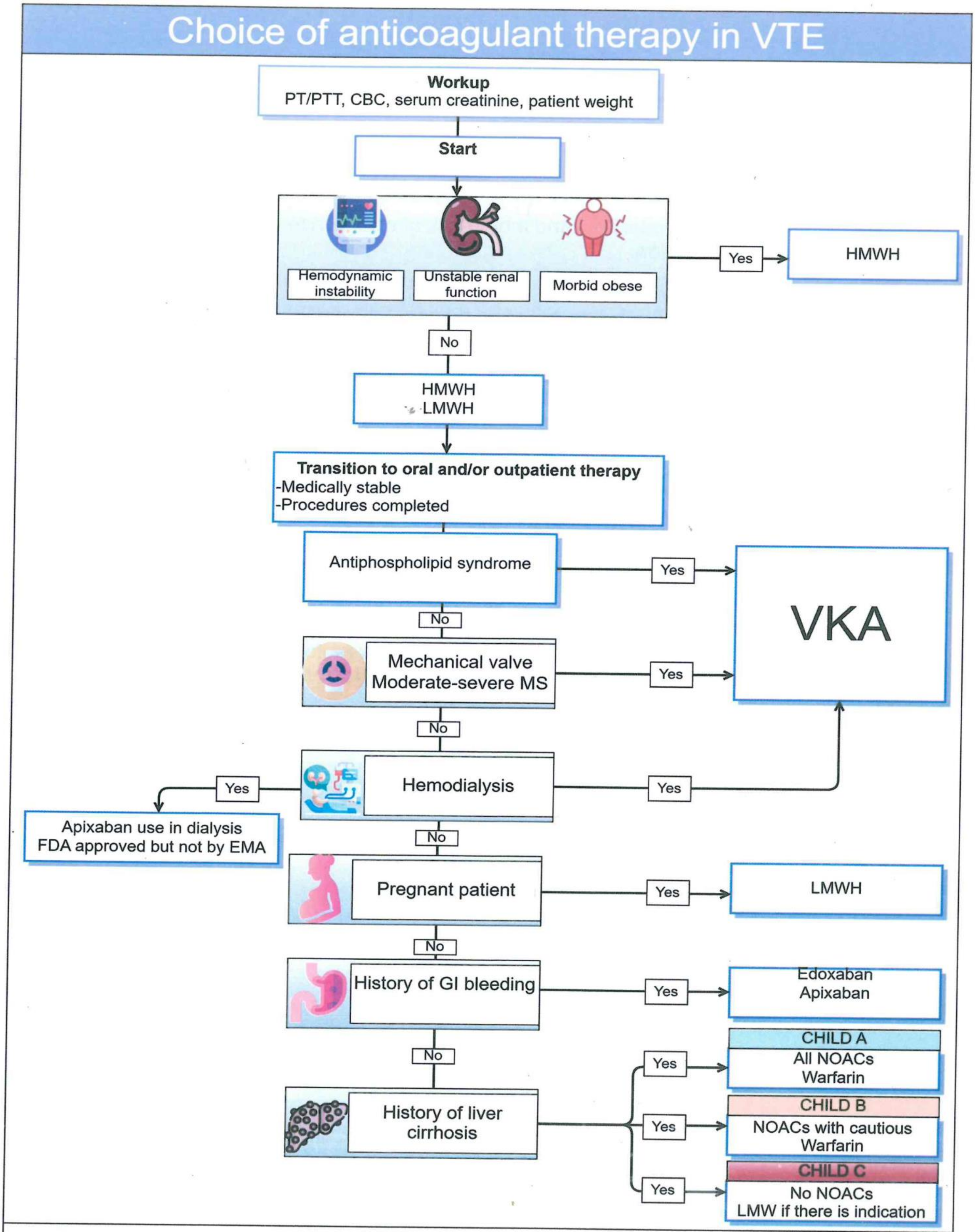
Management of deep venous thrombosis and anticoagulation

General Principles

- Clinical signs and symptoms of acute DVT are highly variable and nonspecific
- Patients with isolated distal DVT and a high risk of recurrence should be treated with 3 months of anticoagulation.
- Patients with proximal DVT should receive at least 3 months of anticoagulation therapy.
- For upper extremity DVT, ultrasound is the diagnostic modality of choice and treatment is similar to lower extremity DVT.
- During pregnancy, LMWH is the recommended anticoagulation for initial and long-term treatment. Anticoagulation should be continued for at least 6 weeks after delivery (for a minimum of 3 months of treatment).
- Various risk prediction models can be used to assess the risk of VTE recurrence. These include the Vienna model, the DASH score, and HERDOO-2.

Anticoagulation Treatment Options

- Patient specific factors should be considered when selecting an anticoagulant.
- The direct oral anticoagulants (apixaban, dabigatran, edoxaban and rivaroxaban) are now considered the preferred agents for treatment of uncomplicated VTE
- Dose adjusted vitamin K antagonist (i.e. warfarin), low molecular weight heparin (LMWH) and high molecular heparin (HMFH) remain therapeutic options and may be preferred in specific clinical scenarios.
- An algorithm for selecting therapy is provided in Figure 38 -1


Choice of anticoagulant therapy in VTE
Workup
PT/PTT, CBC, serum creatinine, patient weight
Start
Hemodynamic instability
Unstable renal function
Morbid obese
Yes
HMWH
No
HMWH
LMWH
Transition to oral and/or outpatient therapy
-Medically stable
-Procedures completed
Antiphospholipid syndrome
Yes
VKA
No
Mechanical valve
Moderate-severe MS
Yes
No
Hemodialysis
Yes
Yes
Apixaban use in dialysis
FDA approved but not by EMA
No
Pregnant patient
Yes
LMWH
No
History of GI bleeding
Yes
Edoxaban
Apixaban
No
History of liver cirrhosis
Yes
CHILD A
All NOACs
Warfarin
Yes
CHILD B
NOACs with cautious
Warfarin
Yes
CHILD C
No NOACs
LMW if there is indication

Beyer-Westendorf J, Köhler C. Direct Oral Anticoagulants: Laboratory Challenges and Antidotes. Hamostaseologie. 2023 Feb;43(1):37-43.
HMWH: high molecular weight heparin, LMWH: low molecular weight heparin, VKA: vitamin K antagonsit

Figure 38-1:Algorithm for selecting anticoagulant therapy

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High Molecular Weight Heparin (HMWH)

- Parenteral agent of choice for patients with renal dysfunction, on renal replacement therapy or when an anticoagulant with a shorter duration of action is needed (i.e. prior to surgical procedure).
- Dose adjustment is listed in Table 38 -1

Table 38-1:Dose adjustment of HMWH for therapeutic anticoagulation

- Bolus dose of 80 III/Kg Followed by continuous infusion of 18 IU/Kg/hr
- Prepared in a 50- ml syringe by diluting one ampoule of heparin on 50 ml normal saline to a final concentration of 100 IU/ml Or 5 ampoules in 50 ml normal saline for fluid restricted patients
- Doses should be calculated using Actual body weight
- Morbidly Obese patients with BMI ≥ 40Kg/m2 , use Adjusted body weight ***(IBW + 0.4 (Actual weight - IBW))***
- Check PTT 6 hours after starting the infusion and adjust the dose as indicated below

PTT (Seconds)	**Bolus dose**	**Continuous infusion**
<35	80 IU/Kg	Increase by 4 IU/Kg/hr
35-40	40 IU/Kg	Increase by 2 IU/Kg/hr
46-70	-	-
71-90	-	Decrease by 2 IU/Kg/hr
>90	-	Stop infusion for 1 hour then decrease by 3 IU/Kg/ hr
Check PTT 6 hours after each dose adjustment , when in desired range (46-70 seconds) , monitor daily		

Low Molecular Weight Heparin

- Agent of choice for treatment of VTE in patients with cancer associated VTE, during pregnancy or for transitioning to warfarin.
- Parenteral agent of choice for rapid therapeutic anticoagulation with an onset of action within 2 hours.
- Dosing and special considerations are listed in Table 38 -2

Table 38-2:Dose and special consideration of LMWH for deep venous thrombosis

Drug	Interval
Enoxaparin Cr Cl ≥ 30 ml/min	1 mg/kg SC / 12 hrs
Enoxaparin Cr Cl < 30 ml/min	1 mg/kg SC / 24 hrs
Enoxaparin Weight > 100 kg or BMI>40 Cr Cl ≥ 30 ml/min	0.8 mg/kg SC / 12 hrs on actual body weight max 150 mg/12 hrs
Fondaparinux Cr Cl ≥ 50 ml/min	• 5 mg (body weight <50 kg)/24 hrs • 7.5 mg (body weight 50-100 kg)/24 hrs • 10 mg (body weight >100 kg)/24 hrs
Fondaparinux Cr Cl < 30 ml/min	Contraindicated
Dalteparin	100 IU/kg every 12 hrs 200 IU/kg /24 hrs

New oral anticoagulant (NOAC)

- NOAC are the preferred treatment option for uncomplicated VTE
- There is no indication for overlap of parenteral anticoagulation with LMWH or UFH
- If using dabigatran or edoxaban for VTE treatment, use of UFH or LMWH for 5-10 days before switching to oral agent is recommended (Parenteral Lead-In)
- Do not use NOAC in the following conditions
    - » Prosthetic heart valves or moderate to severe mitral stenosis
    - » Pediatric patients (age < 18 years)
    - » Pregnant or lactating
    - » Antiphospholipid syndrome
    - » Active GIT malignancy
- Doses and factors that affect NOAC choice are described in Figure 38 -2

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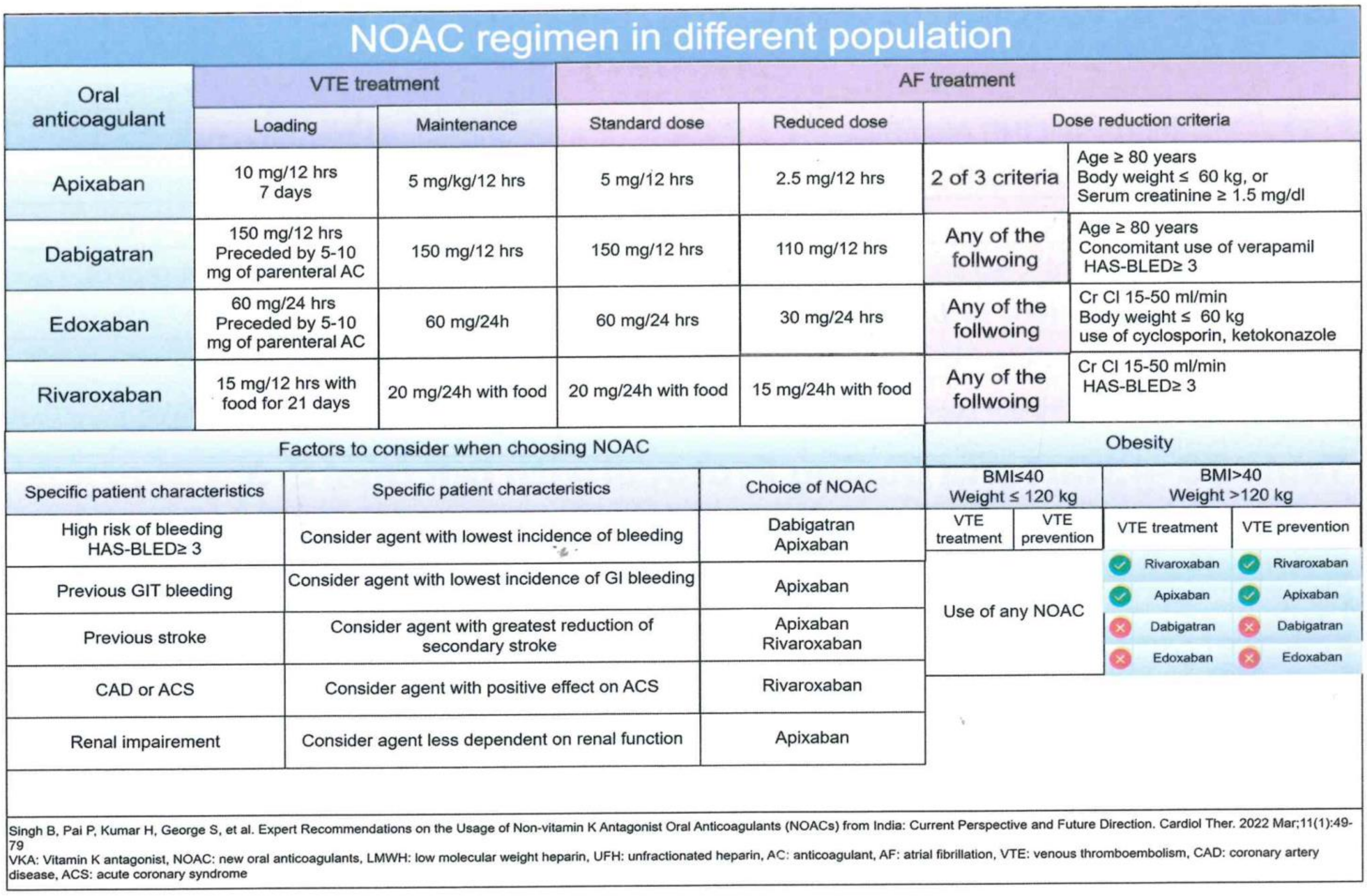

NOAC regimen in different population

Oral anticoagulant	VTE treatment		AF treatment			
	Loading	Maintenance	Standard dose	Reduced dose	Dose reduction criteria	
Apixaban	10 mg/12 hrs 7 days	5 mg/kg/12 hrs	5 mg/12 hrs	2.5 mg/12 hrs	2 of 3 criteria	Age ≥ 80 years Body weight ≤ 60 kg, or Serum creatinine ≥ 1.5 mg/dl
Dabigatran	150 mg/12 hrs Preceded by 5-10 mg of parenteral AC	150 mg/12 hrs	150 mg/12 hrs	110 mg/12 hrs	Any of the follwoing	Age ≥ 80 years Concomitant use of verapamil HAS-BLED≥ 3
Edoxaban	60 mg/24 hrs Preceded by 5-10 mg of parenteral AC	60 mg/24h	60 mg/24 hrs	30 mg/24 hrs	Any of the follwoing	Cr Cl 15-50 ml/min Body weight ≤ 60 kg use of cyclosporin, ketokonazole
Rivaroxaban	15 mg/12 hrs with food for 21 days	20 mg/24h with food	20 mg/24h with food	15 mg/24h with food	Any of the follwoing	Cr Cl 15-50 ml/min HAS-BLED≥ 3

Factors to consider when choosing NOAC

Specific patient characteristics	Specific patient characteristics	Choice of NOAC
High risk of bleeding HAS-BLED≥ 3	Consider agent with lowest incidence of bleeding	Dabigatran Apixaban
Previous GIT bleeding	Consider agent with lowest incidence of GI bleeding	Apixaban
Previous stroke	Consider agent with greatest reduction of secondary stroke	Apixaban Rivaroxaban
CAD or ACS	Consider agent with positive effect on ACS	Rivaroxaban
Renal impairement	Consider agent less dependent on renal function	Apixaban

Obesity

BMI≤40 Weight ≤ 120 kg		BMI>40 Weight >120 kg	
VTE treatment	VTE prevention	VTE treatment	VTE prevention
Use of any NOAC		✓ Rivaroxaban	✓ Rivaroxaban
		✓ Apixaban	✓ Apixaban
		✗ Dabigatran	✗ Dabigatran
		✗ Edoxaban	✗ Edoxaban

Singh B, Pai P, Kumar H, George S, et al. Expert Recommendations on the Usage of Non-vitamin K Antagonist Oral Anticoagulants (NOACs) from India: Current Perspective and Future Direction. Cardiol Ther. 2022 Mar;11(1):49-79

VKA: Vitamin K antagonist, NOAC: new oral anticoagulants, LMWH: low molecular weight heparin, UFH: unfractionated heparin, AC: anticoagulant, AF: atrial fibrillation, VTE: venous thromboembolism, CAD: coronary artery disease, ACS: acute coronary syndrome

Figure 38-2:NOAC regimen in different population

Warfarin

- Preferred oral anticoagulant option for patients who are not candidates for NOAC therapy.
- Due to delayed onset of action, overlap of parenteral anticoagulation with either LMWH or UFH should occur for at least 5 days AND until the INR > 2 of two consecutive INRs
- Warfarin should be started on the same day as parenteral anticoagulation.
- A baseline INR should be resulted prior to initiating warfarin therapy.
- Patients newly started on warfarin should be assessed for risk factors that may make them more sensitive to the effects of warfarin. If multiple high sensitivity risk factors are present, then a lower initiation dose or reduced maintenance dose may be needed (Table 38-3)
- Recommendations for warfarin dosing in the first 5 days of therapy for INR goals of 2-3 (Table 38-4)
- For enteral nutrition hold the tube feed 1 hour before and 1 hour after warfarin administration
- Medications, dietary supplements and food that interact with warfarin is mentioned in Table 38 -5

Table 38-3: Factors for Identifying Warfarin Sensitive Patients

Increased Warfarin Sensitivity	
Increased INR response	Increased bleeding risk
Baseline INR ≥ 1.5	Current antiplatelet therapy
Age > 65	Thrombocytopenia: platelet <75 K/uL
Actual body weight < 45 kg or actual < ideal	cirrhosis or total bilirubin.>2.4 mg/dL
Malnourished/ NPO >3 days	Alcohol abuse history
Hypoalbuminemia <2 g/dL	End stage renal disease
Decompensated heart failure	GI bleed within past 50 days

Table 38-4:Warfarin Dosing Protocol with INR Goal 2-3

	High Sensitivity to Warfarin		Low Sensitivity to Warfarin	
	INR Value	Dose	INR Value	Dose
Day 1	<1.5	2.5 – 5 mg	<1.5	5 – 7.5 mg
Day 2	<1.5 ≥1.5	2.5 – 5 mg 0 – 2.5 mg	<1.5 ≥1.5	5 – 7.5 mg 0 – 5 mg
Day 3	<1.5 1.5–1.9 2–2.5 ≥2.6	5 mg 2.5 mg 1 mg 0 (no dose)	<1.5 1.5–1.9 2–2.5 ≥2.6	7.5 mg 5 mg 2.5 mg 0 (no dose)
Day 4	<1.5 1.5–1.9 2–3 > 3	7.5 mg 5 mg 2.5 mg 0 – 1 mg	<1.5 1.5–1.9 2–3 >3	10 mg 7.5 mg 5 mg 0–2.5 mg
Day 5	<1.5 1.5–1.9 2–3 3–3.5 >3.5	10 mg yesterday's dose + 1 mg yesterday's dose yesterday's dose – 1 mg 0 (no dose)	<1.5 1.5–1.9 2–3 3–3.5 >3.5	12.5 mg yesterday's dose + 2.5 mg yesterday's dose yesterday's dose – 2.5 mg 0 (no dose)

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Table 38-5:Medications, dietary supplements and food that interact with warfarin

Drug class	Interactions increase INR and bleeding	Interactions decrease INR
Anti-Infective	Ciprofloxacin - Erythromycin Fluconazole - Isoniazid Metronidazole - Moxifloxacin Sulfamethoxazole - Voriconazole	Griseofulvin Nafcillin Ribavirin Rifampin
Cardiovascular	Amiodarone - Clofibrate Diltiazem - Fenofibrate Propafenone - Propranolol	Cholestyramine
Analgesics, Anti-Inflammatory	Piroxicam	
CNS Drugs	Alcohol - Citalopram Entacapdne - Sertraline	Barbiturates Carbamazepine
GI Drugs and Food	Cimetidine - Mango Omeprazole	High content vitamin K food Avocado
Herbal Supplement	Fenugreek - Feverfew Fish Oil - Ginkgo - Guilinggao	Alfalfa
Other	Anabolic Steroids Capecitabine - Zileuton	Mercaptopurine Chewing Tobacco

How to Switch Between Different Anticoagulant Regimen

Conversion Among Parenteral Anticoagulants

Table 38-6:Conversion among parenteral anticoagulants

	To IV heparin	To SC heparin q12	To IV Bivalirudin	To LMWH q24	To LMWH q12	To Fondaparinux
From IV heparin		Stop IV heparin and start SC heparin at the same time	Stop IV heparin and start IV bivalirudin at the same time	Stop IV heparin and start LMWH at the same time	Stop IV heparin and start LMWH at the same time	Stop IV heparin and start fondaparinux at the same time
SC heparin q 12	Stop SC heparin and start IV heparin 4 hours before the next dose of SQ heparin would have been given		Stop SC heparin and start IV Bivalirudin 2 hours before the next dose of SC heparin would have been given	Stop SC heparin and start LMWH at the time next dose of SC heparin would have been given	Stop SC heparin and start LMWH at the time next dose of SC heparin would have been given	Stop SC heparin and start fondaparinux at the time next dose of SC heparin would have been given
From IV Bivalirudin	Stop bivalirudin and start IV heparin at the same time	Stop bivalirudin and start SC heparin at the same time		Stop bivalirudin and start LMWH at the same time	Stop bivalirudin and start LMWH at the same time	Stop bivalirudin and start fondaparinux at the same time
LMWH SC / 24 hrs	Stop LMWH and start IV heparin 4 hours before the next dose of LMWH would have been given	Stop LMWH and give first dose of SC heparin at the time the next dose of LMWH would have been given	Stop LMWH and start IV bivalirudin 2 hours before the next dose of LMWH would have been given		Give next dose of LMWH 12 hours after the last dose was given	Stop LMWH and give first dose of fondaparinux at the time the next dose of LMWH would have been given
LMWH Sc/ 12 hrs	Stop LMWH and start IV heparin 4 hours before the next dose of LMWH would have been given	Stop LMWH and give first dose of SC heparin at the time the next dose of LMWH would have been given	Stop LMWH and start IV bivalirudin 2 hours before the next dose of LMWH would have been given	Give next dose of LMWH 24 hours after the last dose was given		Stop LMWH and give first dose of fondaparinux at the time the next dose of LMWH would have been given
Fondaparinux	Stop Fondaparinux and start IV heparin 4 hours before the next dose of Fondaparinux would have been given	Stop fondaparinux and give first dose of SC heparin at the time the next dose of fondaparinux would have been given	Stop fondaparinux and start IV bivalirudin 2 hours before the next dose of fondaparinux would have been given	Stop fondaparinux and give first dose of LMWH at the time the next dose of fondaparinux would have been given	Stop fondaparinux and give first dose of LMWH at the time the next dose of fondaparinux would have been given	

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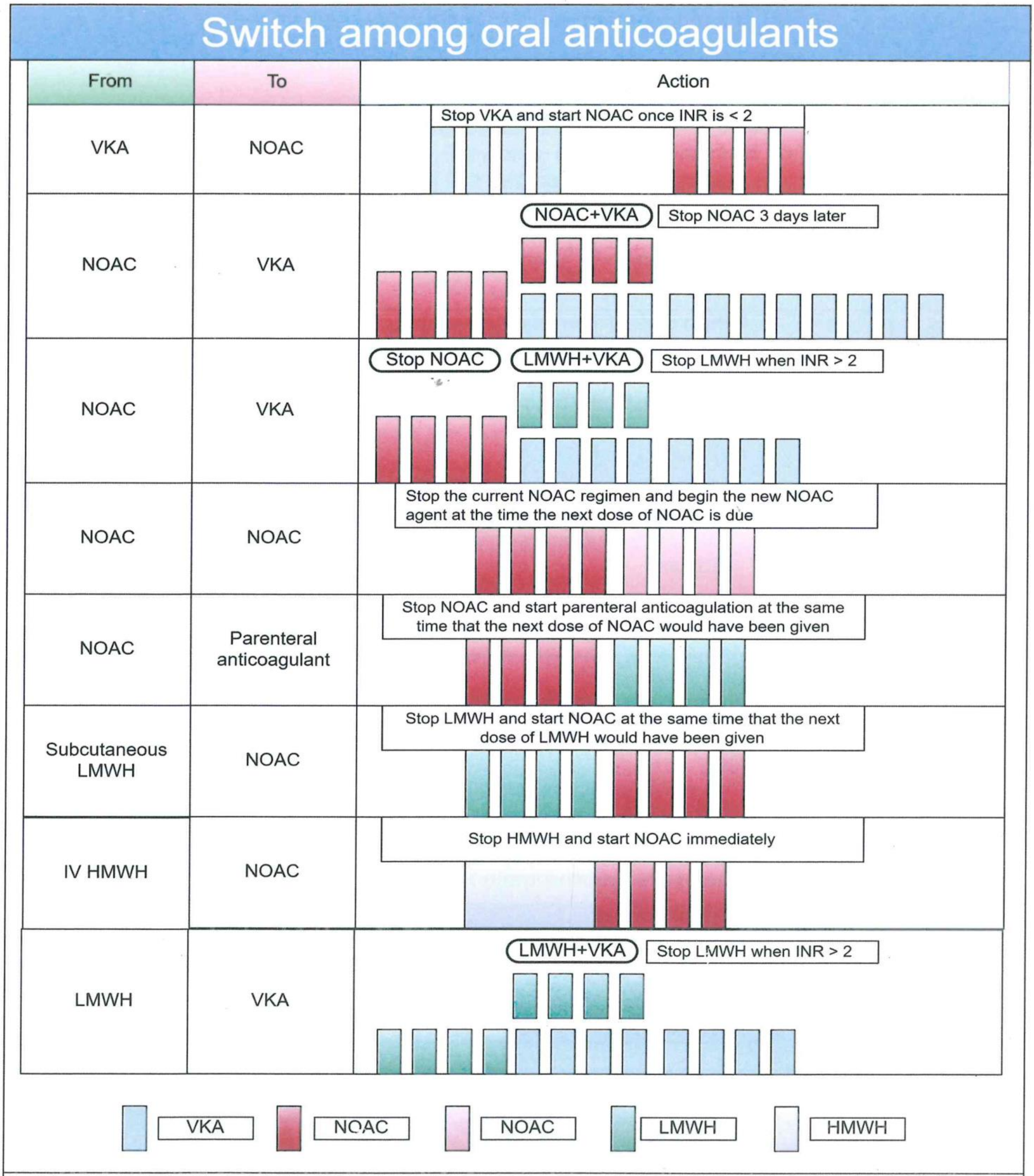
Conversion Among Oral Anticoagulants



Switch among oral anticoagulants

From	To	Action
VKA	NOAC	Stop VKA and start NOAC once INR is < 2
NOAC	VKA	NOAC+VKA Stop NOAC 3 days later
NOAC	VKA	Stop NOAC LMWH+VKA Stop LMWH when INR > 2
NOAC	NOAC	Stop the current NOAC regimen and begin the new NOAC agent at the time the next dose of NOAC is due
NOAC	Parenteral anticoagulant	Stop NOAC and start parenteral anticoagulation at the same time that the next dose of NOAC would have been given
Subcutaneous LMWH	NOAC	Stop LMWH and start NOAC at the same time that the next dose of LMWH would have been given
IV HMWH	NOAC	Stop HMWH and start NOAC immediately
LMWH	VKA	LMWH+VKA Stop LMWH when INR > 2

Abo-Salem E, Becker R. Transitioning to and from the novel oral anticoagulants: a management strategy for clinicians. J Thromb Thrombolysis. 2014 Apr;37(3):372-9
HMWH: high molecular weight heparin, LMWH: low molecular weight heparin, VKA: vitamin K antagonsit, NOAC: new oral anticoagulant

Figure 38-3: conversion among oral anticoagulants

Reversal of Anticoagulants

- Details of reversal of anticoagulant are discussed in Table 38 -7

Table 38-7:Reversal of anticoagulants

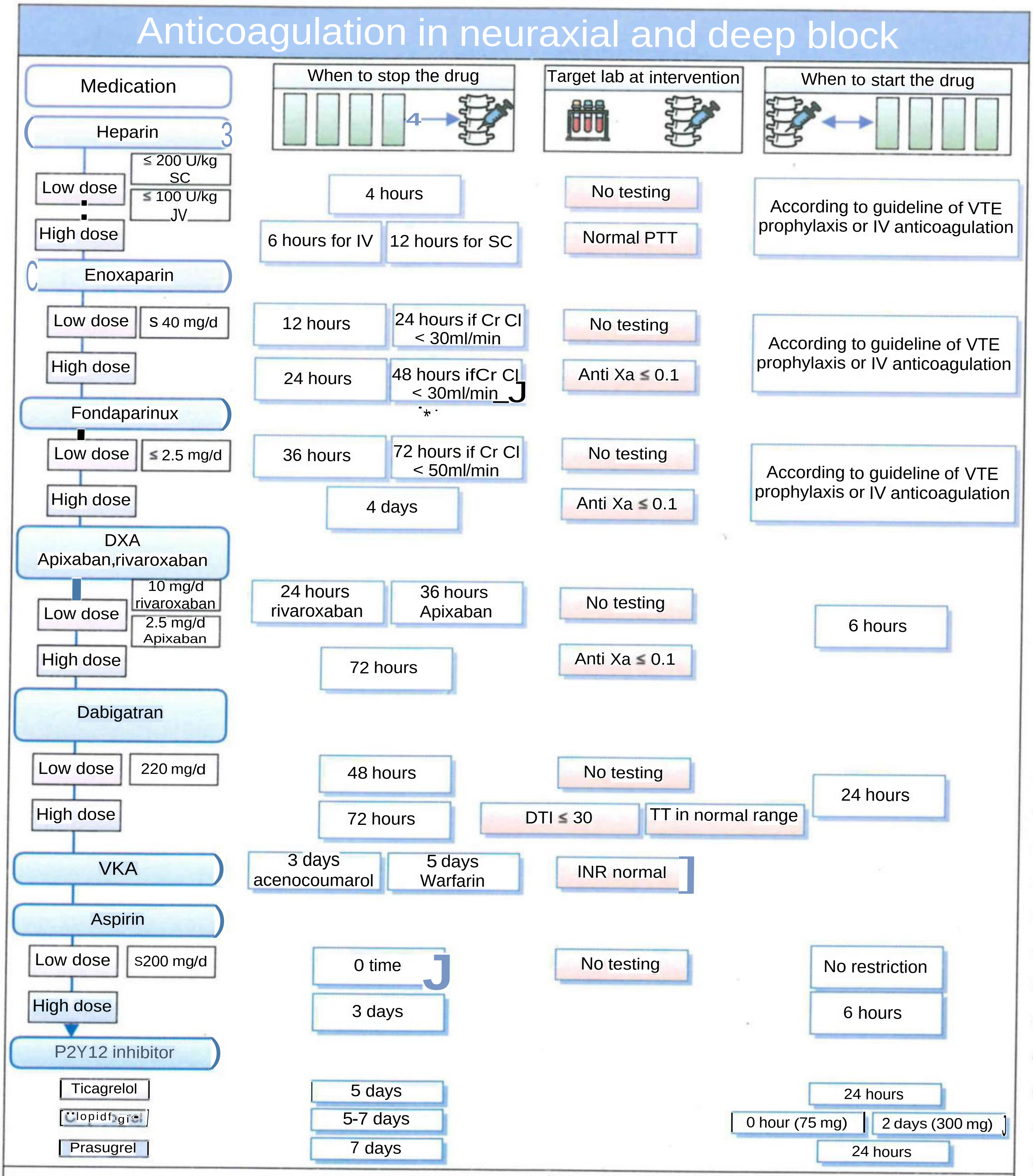
<table>
<tr><th>Drug</th><th>First line</th><th>Second line</th></tr>
<tr><td>Apixaban
(Eliquis)

Rivaroxaban
(Xarelto)</td><td>• Andexanet alfa (On-dexxya ®)
» Low dose: Rivaroxaban ≤10 mg, apixaban ≤5 mg, Elapsed time >8 h regardless of dose: bolus 400 mg at 30 mg/ min, then infusion 480 mg at 4 mg/min
» High dose: Rivaroxaban >10 mg; apixaban >5 mg with elapsed time <8 h: bolus 800 mg at 30 mg/min, then infusion 960 mg at 8 mg/min</td><td>• PCC 2100–3500 IU (30 or 50 IU/kg)
• rFVIIa (Novoseven ®) 6300 pg administered over 5 min (90 pg/kg)
• FXIII (Fibrogammin ®) 1050–1400 IU maximum dose 250 IU/min</td></tr>
<tr><td>Dabigatran
(Pradaxa)</td><td>• Idarucizumab (Praxbind ®)
» 2 boluses of 2.5 mg at 15 min interval</td><td>• PCC 2100–3500 IU (30 or 50 IU/kg)
• rFVIIa (Novoseven ®) 6300 pg administered over 5 min (90 pg/kg)
• FXIII (Fibrogammin ®) 1050–1400 IU maximum dose 250 IU/min</td></tr>
<tr><td>VKA</td><td>• Vitamin K (Phytomenadione, Konakion ®)
» 10 mg IV over 20 minutes
• PCC
» If no INR available: 1750 IU (25 IU/kg)
» body weight x 40 x [Targeted - measured prothrombin rate]/100
<table>
<tr><th>Baseline INR</th><th>Dose of PCC in IU/kg</th></tr>
<tr><td>2-4</td><td>25</td></tr>
<tr><td>4-6</td><td>30</td></tr>
<tr><td>>6</td><td>50</td></tr>
</table></td><td>• FFP 700–1050 ml total (10–15 ml/kg)</td></tr>
<tr><td>Heparin</td><td colspan="2">• Use protamine for heparin neutralization (100%)
<table>
<tr><th>Time since last dose of Heparin</th><th>Dose of protamine for each 100 units of heparin administered</th></tr>
<tr><td>Immediate</td><td>1mg (or 25 mg fixed dose)</td></tr>
<tr><td>30 min-2 hrs</td><td>0.5mg (or 10mg fixed dose)</td></tr>
<tr><td>> 2hrs</td><td>0.25mg (or 10mg fixed dose)</td></tr>
</table></td></tr>
</table>

<table>
<tr><td>fondaparinux
(Arixtra)</td><td>• No specific antidote</td><td>• PCC 1000 IU
• rFVIIa (Novoseven ®) 6300 (jg administered over 5 min [90 pg/kg)</td></tr>
<tr><td>Enoxaparin
(Clexan)</td><td colspan="2" rowspan="2">• Use protamine for partial neutralization (-60%)
<table>
<tr><th>Time since last dose of LMWH</th><th>Dose of protamine for each 100 units of dalteparin or 1mg of enoxaparin administered</th></tr>
<tr><td>< 8 hrs</td><td>1mg (or 50mg fixed dose)</td></tr>
<tr><td>8-12 hrs</td><td>0.5mg (or 25mg fixed dose)</td></tr>
<tr><td>> 12hrs</td><td>Not likely to be useful (or 25mg fixed dose)</td></tr>
</table></td></tr>
<tr><td>Dalteparin
(Fragmin)</td></tr>
</table>

Anticoagulation management in neuroaxial and deep nerve block

- Anticoagulant management for neuraxial and peripheral nerve block is illustrated in Figure 38 -4
- Examples of deep block is described in Table 38 -8



Anticoagulation in neuraxial and deep block

Medication		When to stop the drug	Target lab at intervention	When to start the drug
Heparin				
Low dose	≤ 200 U/kg SC	4 hours	No testing	According to guideline of VTE prophylaxis or IV anticoagulation
High dose	≤ 100 U/kg JV	6 hours for IV 12 hours for SC	Normal PTT	
Enoxaparin				
Low dose	≤ 40 mg/d	12 hours 24 hours if Cr Cl < 30ml/min	No testing	According to guideline of VTE prophylaxis or IV anticoagulation
High dose		24 hours 48 hours ifCr Cl < 30ml/min	Anti Xa ≤ 0.1	
Fondaparinux				
Low dose	≤ 2.5 mg/d	36 hours 72 hours if Cr Cl < 50ml/min	No testing	According to guideline of VTE prophylaxis or IV anticoagulation
High dose		4 days	Anti Xa ≤ 0.1	
DXA Apixaban,rivaroxaban				
Low dose	10 mg/d rivaroxaban 2.5 mg/d Apixaban	24 hours rivaroxaban 36 hours Apixaban	No testing	6 hours
High dose		72 hours	Anti Xa ≤ 0.1	
Dabigatran				
Low dose	220 mg/d	48 hours	No testing	24 hours
High dose		72 hours	DTI ≤ 30 TT in normal range	
VKA		3 days acenocoumarol 5 days Warfarin	INR normal	
Aspirin				
Low dose	≤200 mg/d	0 time	No testing	No restriction
High dose		3 days		6 hours
P2Y12 inhibitor				
Ticagrelol		5 days		24 hours
Clopidogrel		5-7 days		0 hour (75 mg) 2 days (300 mg)
Prasugrel		7 days		24 hours

Kietaibl S, Ferrandis R, Godier A, et al.Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. Eur J Anaesthesiol. 2022;39(2):100-132
PTT, activated partial thromboplastin time; CrCl, creatinine clearance; DTI, direct thrombin inhibitor; DXA, direct Xa antagonist, INR, International Normalised Ratio; subcutaneous; UFH, unfractionated heparin; VKA, Vitamin K antagonist

Figure 38-4:Anticoagulation for neuraxial and deep peripheral nerve block

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Table 38-8: Superficial and deep peripheral nerve block

Deep block	Superficial block
Head, neck	
Stellate ganglion Deep cervical plexus Cervical paravertebral	Occipital Peribulbar Sub-Tenon's Superficial cervical plexus
Upper limb	
Infraclavicular	Interscalene Supraclavicular Axillary Suprascapular Ulnar, radial, medial (forearm or wrist level)
Thorax	
Epidural Thoracic paravertebral	Parasternal intercostal plane (deep, superficial) Serratus anterior (deep, superficial) Erector spinae plane Intercostal Interpectoral plane and pecto-serratus plane
Abdomen, pelvic	
	Ilioinguinal Iliohypogastric Transversus abdominis plane (TAP) Rectus sheath Genital branch of genitofemoral nerve Pudendal nerve
Lower limb	
back Lumbar plexus Psoas compartment Lumbar sympathectomy Lumbar paravertebral Quadratus lumborum Fascia transversalis Sacral plexus Pericapsular nerve group (PENG) Sciatic (proximal approaches) Spinal Epidural Lumbar paravertebral	Femoral Femoral triangle Adductor canal Sciatic (subgluteal, popliteal level) Fascia iliaca Lateral cutaneous nerve of the thigh Femoral branch of genitofemoral nerve Sural, saphenous, tibial, peroneal (deep, superficial)

Perioperative management of anticoagulation

- Risk stratification for perioperative anticoagulation depends on the balance between risk of bleeding and risk of thrombosis
- Bleeding risk is classified according to intervention into minimal, mild to moderate, and high risks.
- Thrombotic risk is classified into high moderate and low risk of thrombosis Table 38 -9
- Warfarin interruption with or without bridging therapy depend on the balance between thrombotic and bleeding risk. Figure 38 -5
- NOAC interruption depends on the types of drug and bleeding risk. Figure 38 -5
- Aspirin is continued without interruption. Figure 38-6
- P2Y12 inhibitors is interrupted from 3 to 7 days according to type of therapy

Table 38-9:Risk stratification for use of bridge therapy

Risk Stratum and Recommendations for Use of Bridge Therapy	Mechanical valve	Atrial Fibrillation	Venous thrombosis (VTE)
HIGH RISK	• Any caged ball or tilting valve in mitral or in aortic position • Any mitral valve with prior stroke or valve thrombosis • Recent stroke or TIA (<3 m)	• CHA2DS 2VASC score of ≥ 7 • Recent stroke or TIA (<3 m) • Rheumatic valvular heart disease	• Recent VTE (< 3mo) • Severe thrombophilia (deficiency of protein C, S, and antithrombin III) • Antiphospholipid antibodies • Active cancer with high VTE
MODERATE RISK	• Bileaflet aortic valve replacement (AVR) with major risk factors for stroke (prior stroke or valve thrombosis)	• CHA2DS 2VASc score 5 or 6	• VTE within past 3-12 mo • Recurrent VTE • Heterozygous factor V Leiden • Active cancer
LOW RISK	• Bileafiet aortic valve replacement (AVR) without major risk factors for stroke (prior stroke or valve thrombosis)	• CHA2DS 2VASc score 1 or 4	• VTE > 12 mo

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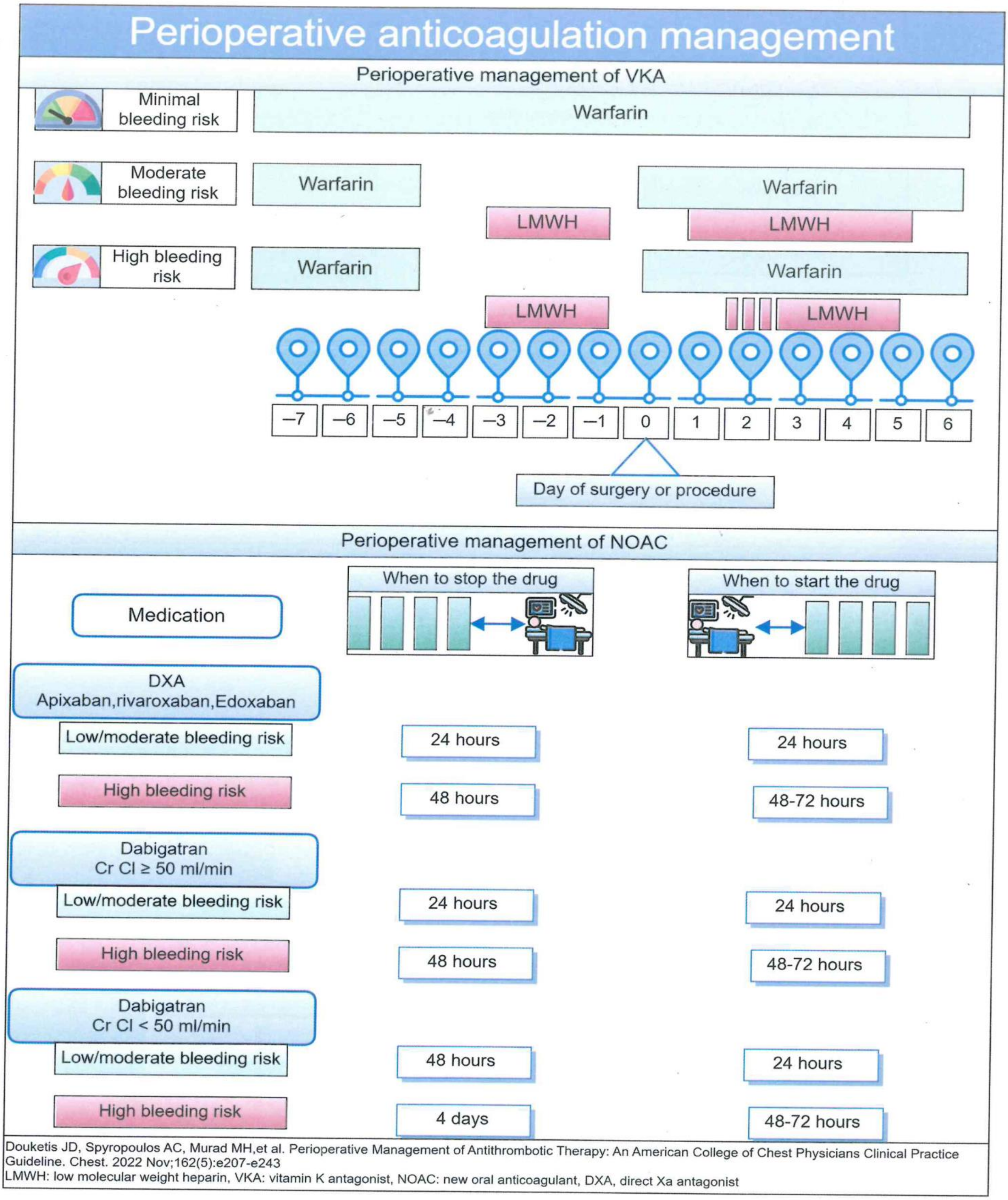


Perioperative anticoagulation management

Perioperative management of VKA

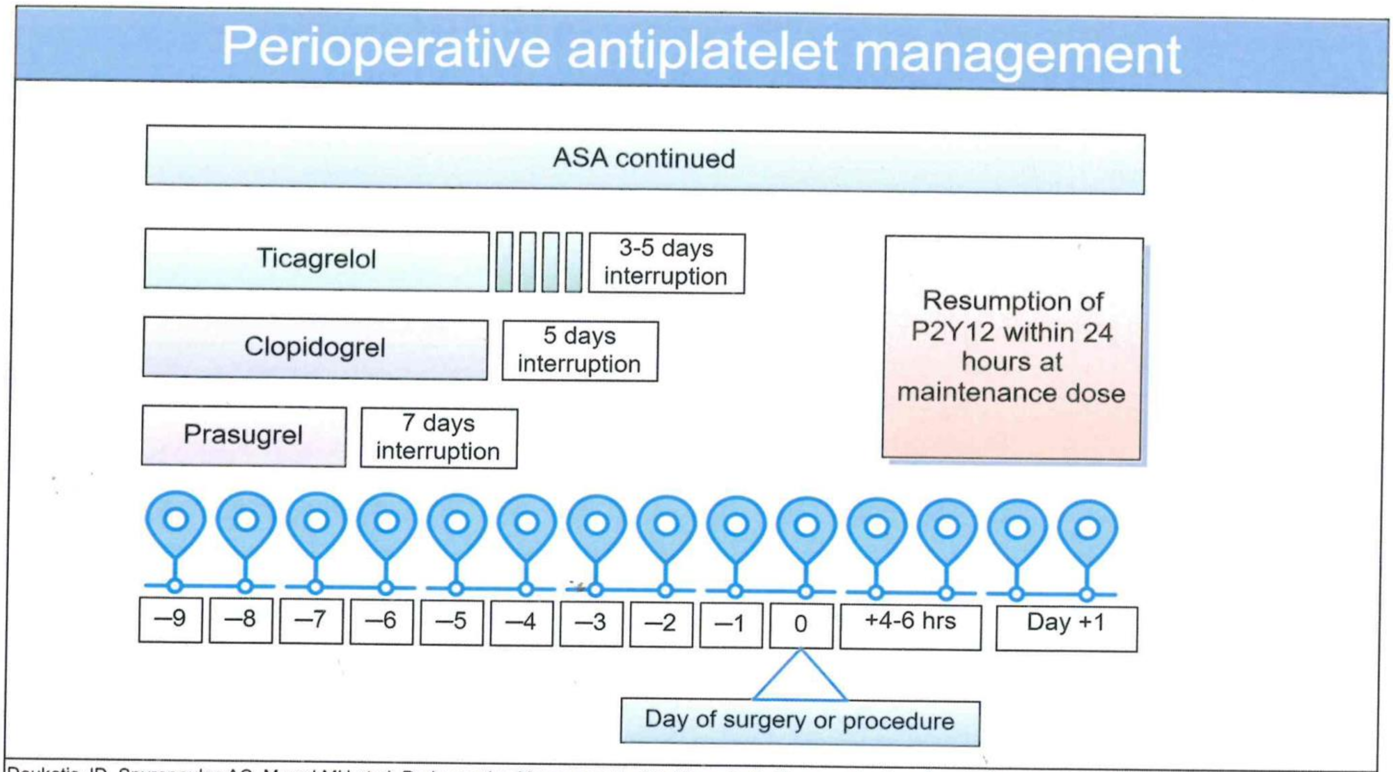
Minimal bleeding risk
Warfarin
Moderate bleeding risk
Warfarin
LMWH
Warfarin
LMWH
High bleeding risk
Warfarin
LMWH
Warfarin
LMWH
–7
–6
–5
–4
–3
–2
–1
0
1
2
3
4
5
6
Day of surgery or procedure

Perioperative management of NOAC

Medication	When to stop the drug	When to start the drug
DXA **Apixaban,rivaroxaban,Edoxaban**		
Low/moderate bleeding risk	24 hours	24 hours
High bleeding risk	48 hours	48-72 hours
Dabigatran **Cr Cl ≥ 50 ml/min**		
Low/moderate bleeding risk	24 hours	24 hours
High bleeding risk	48 hours	48-72 hours
Dabigatran **Cr Cl < 50 ml/min**		
Low/moderate bleeding risk	48 hours	24 hours
High bleeding risk	4 days	48-72 hours

Douketis JD, Spyropoulos AC, Murad MH,et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022 Nov;162(5):e207-e243
LMWH: low molecular weight heparin, VKA: vitamin K antagonist, NOAC: new oral anticoagulant, DXA, direct Xa antagonist

Figure 38-5: Perioperative anticoagulation management


Perioperative antiplatelet management
ASA continued
Ticagrelol
3-5 days interruption
Clopidogrel
5 days interruption
Prasugrel
7 days interruption
Resumption of P2Y12 within 24 hours at maintenance dose
−9
−8
−7
−6
−5
−4
−3
−2
−1
0
+4-6 hrs
Day +1
Day of surgery or procedure

Douketis JD, Spyropoulos AC, Murad MH,et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022 Nov;162(5):e207-e243
ASA: Aspirin,

Figure 38-6: Perioperative antiplatelet management

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References

1. Kietaibl S, Ferrandis R, Godier A, et al. A. Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. Eur J Anaesthesiol. 2022 Feb 1;39(2):100–132
2. Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022;162(5):e207–e243
3. Singh B, Pai P, Kumar H, et al. Expert Recommendations on the Usage of Non-vitamin K Antagonist Oral Anticoagulants (NOACs) from India: Current Perspective and Future Direction. Cardiol Ther. 2022 Mar;11(1):49–79

SECTION 9

Coagulopathy and anemia

Chapter 39

Thrombocytopenia

General Principles

- Thrombocytopenia (defined as a platelet count < 100,000 pL −1) is a common problem in ICU patients
- A platelet count of less than 100,000 pL−1 is seen in 20–50 % of ICU patients

Causes of Thrombocytopenia

The most common causes of thrombocytopenia in intensive care are:

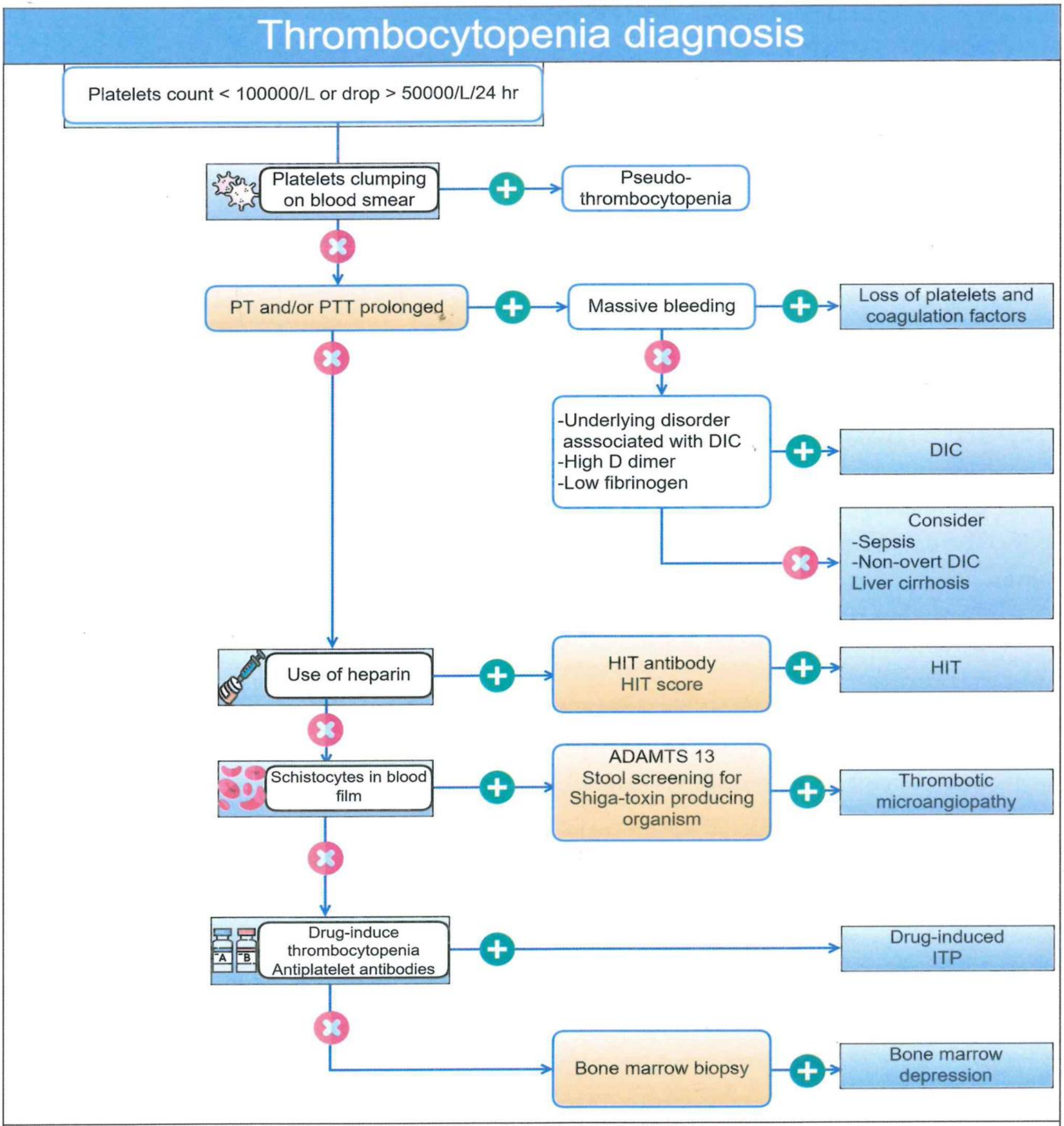
- Pseudothrombocytopenia
- Dilutional thrombocytopenia
- Increase platelet clearance
  - » Sepsis is the major cause of thrombocytopenia in intensive care
  - » Consumptive coagulopathy (DIC) due to liver failure, HELP syndrome, abruption placentae
  - » Microangiopathic hemolytic anemia i.e. Thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS)
  - » Immune thrombocytopenias
  - » Idiopathic (ITP)
  - » Heparin induced thrombocytopenia (HIT)
  - » Drug induced. Table 39 -1
- Increase platelets sequestration.
  - » Cirrhosis and portal hypertension.

Table 39-1: Drugs associated with thrombocytopenia

Antimicrobial	Anticonvulsants	Diuretics	Others
• Linezolid	• Phenytoin	• Furosemide	• Alcohol
• Vancomycin	• Carbamazepine	• Thiazides	• Phenylbutazone
• Fuoroquinolones		• Ethacrynic acid	• Aspirin
• Amphotericin			• Gold salts
• Tetracyclines			• Colchicine
• Sulfonamides			• Chlorpromazine
• Penicillins			• Chlordiazepoxide
• Chloramphenicol			• H2 blockers
• Cephalosporins			

Diagnosis of The Causes of Thrombocytopenia

- The differential diagnosis of thrombocytopenia in critically ill patient is described in Figure 39 -1


Thrombocytopenia diagnosis
Platelets count < 100000/L or drop > 50000/L/24 hr
Platelets clumping on blood smear
Pseudo-thrombocytopenia
PT and/or PTT prolonged
Massive bleeding
Loss of platelets and coagulation factors
-Underlying disorder asssociated with DIC
-High D dimer
-Low fibrinogen
DIC
Consider
-Sepsis
-Non-overt DIC
Liver cirrhosis
Use of heparin
HIT antibody
HIT score
HIT
Schistocytes in blood film
ADAMTS 13
Stool screening for Shiga-toxin producing organism
Thrombotic microangiopathy
A
B
Drug-induce thrombocytopenia
Antiplatelet antibodies
Drug-induced ITP
Bone marrow biopsy
Bone marrow depression

Levi M, Opal SM. Coagulation abnormalities in critically ill patient. Critical care 2006; 10:12

Figure 39-1: Differential diagnosis of thrombocytopenia

Protocol of Platelet Transfusion

Table 39-2: indications for platelet transfusion

Indication	Transfusion Trigger
• Prophylactic use pre-procedure » Surgery involving critical sites (brain-eye) » Non critical site surgery (laparotomy)	 **≤100.000** ≤50.000
• Epidural anesthesia, gastroscopy and biopsy, transbronchial biopsy, liver biopsy	≤50.000
• Routine prophylactic use to reduce bleeding	**<10.000**
• Lumbar puncture	<20.000
• Prophylactic use in patients with additional risk factors e.g. sepsis	10.000-20.000
• Surgery active bleeding	< 50.000
• Stable non bleeding with minor procedure	< 20.000

Heparin-Induced Thrombocytopenia (HIT)

- HIT is the descriptive name of the syndrome heralded by the occurrence of a decreasing platelet count
- The estimated prevalence of HIT in intensive care is 1%

Types

- Type I: is a nonimmunologic response to heparin that leads to an early (48-72 hours) thrombocytopenia that is mediated by a direct interaction between heparin with circulating platelets
- Type II: is an immunologic disorder and associated with venous or arterial thrombosis

Assessment

- Assessment of HIT probability is described in Figure 39 -2

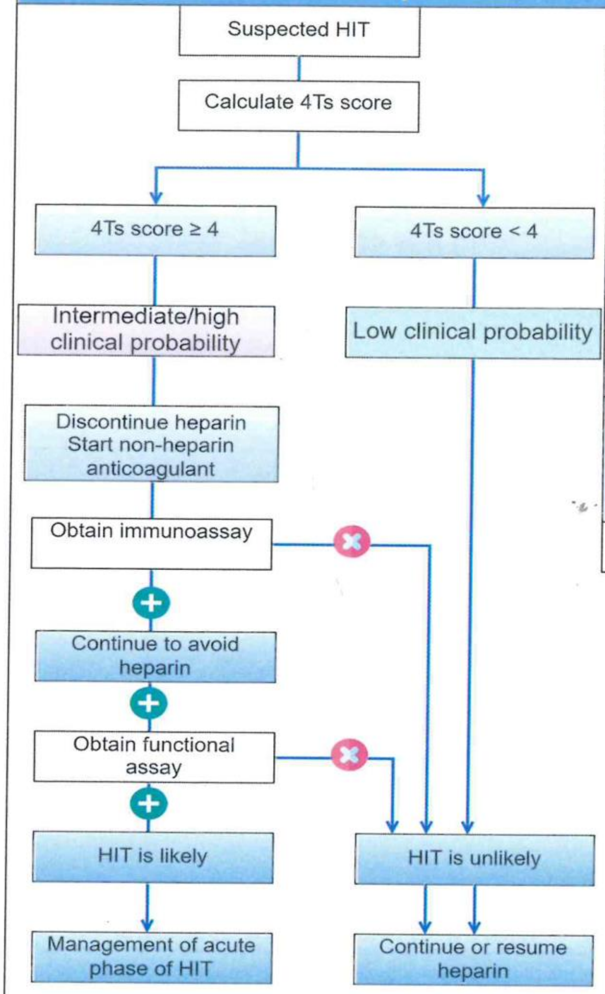
Management

- If HIT is suspected, all heparin products must immediately be discontinued
- Non-heparin anticoagulant treatment options are described in Table 39-3

Table 39-3: Non-heparin anticoagulants

Fondaparinux	
Cr Cl > 30 ml//min Total body weight (kg)	**Dose**
< 50	**5 mg SC/24 hr**
50-100	**7.5 mg SC/24 hrs**
>100	**10 mg SC/24 hrs**
Argatroban	
Indication for dose adjustment	**Initial infusion rate**
Normal liver function	**2 pg/kg/min**
Critically ill	**1 pg/kg/min**
CHILD B liver cirrhosis	**0.5 pg/kg/min**
CHILD C liver cirrhosis, ECMO, or heart failure	**0.25 pg/kg/min**
Bivalirudin initial infusion	
Estimated creatinine clearance	**Initial Bivalirudin Infusion Rate (mg/kg/hr)**
> 60	**0.15**
30-60	**0.08**
< 30 or renal replacement therapy	**0.05**
Bivalirudin infusion rate adjustments	
PTT (Seconds)	**Dose adjustment**
< 1.5 X baseline	**Increase infusion by 20%**
1.5-2.5 X baseline	**Continue current rate**
>2.5-3 X baseline	**Decrease infusion by 20%**
> 3 X baseline	**Hold for 1 hour, then restart at 50% lower rate.**

Heparin-induced thrombocytopenia


Suspected HIT
Calculate 4Ts score
4Ts score ≥ 4
4Ts score < 4
Intermediate/high clinical probability
Low clinical probability
Discontinue heparin Start non-heparin anticoagulant
Obtain immunoassay
+
Continue to avoid heparin
+
Obtain functional assay
+
HIT is likely
HIT is unlikely
Management of acute phase of HIT
Continue or resume heparin

4 Ts score			
4Ts	2 points	1 point	0 point
Thrombocytopenia	PLT fall > 50% AND nadir ≥ 20 k AND no surgery within previous 3 days	PLT fall > 50% but surgery within previous 3 days PLT fall 30-50% or nadir 10-19 k	PLT fall < 30% Any PLT fall with nadir < 10 k
Timing of PLT count fall	Fall 5-10 days after heparin Fall within 1 day if prior exposure within 30 days	>Day 10 or timing not clear (missing platelet counts) ≤ day 1 with prior heparin exposure within the last 30–100 days	< Day 4 without recent exposure
Thrombosis or other sequelae	Confirmed new thrombosis, skin necrosis, or acute systemic reaction after IV heparin bolus	Progressive or recurrent thrombosis, erythematous skin lesions, or suspected thrombosis (not proven)	Thrombosis suspected
Other causes of thrombocytopenia	No alternative explanation for platelet fall	Sepsis without proven source Thrombocytopenia associated with initiation of ventilator	Within 72 hrs. of surgery Confirmed bacteremia or fungemia DIC due to non-HIT cause Post-transfusion purpura Drug induced

0-3: Low HIT probability | 4-5: intermediate HIT probability | 6-8: High HIT probability

Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. Blood Adv. Nov 27 2018;2(22):3360-3392.
PLT: platelets, HIT: heparin-induced thrombocytopenia

Figure 39-2: Diagnosis and initial management of suspected HIT

Thrombotic Thrombocytopenic Purpura

General principles

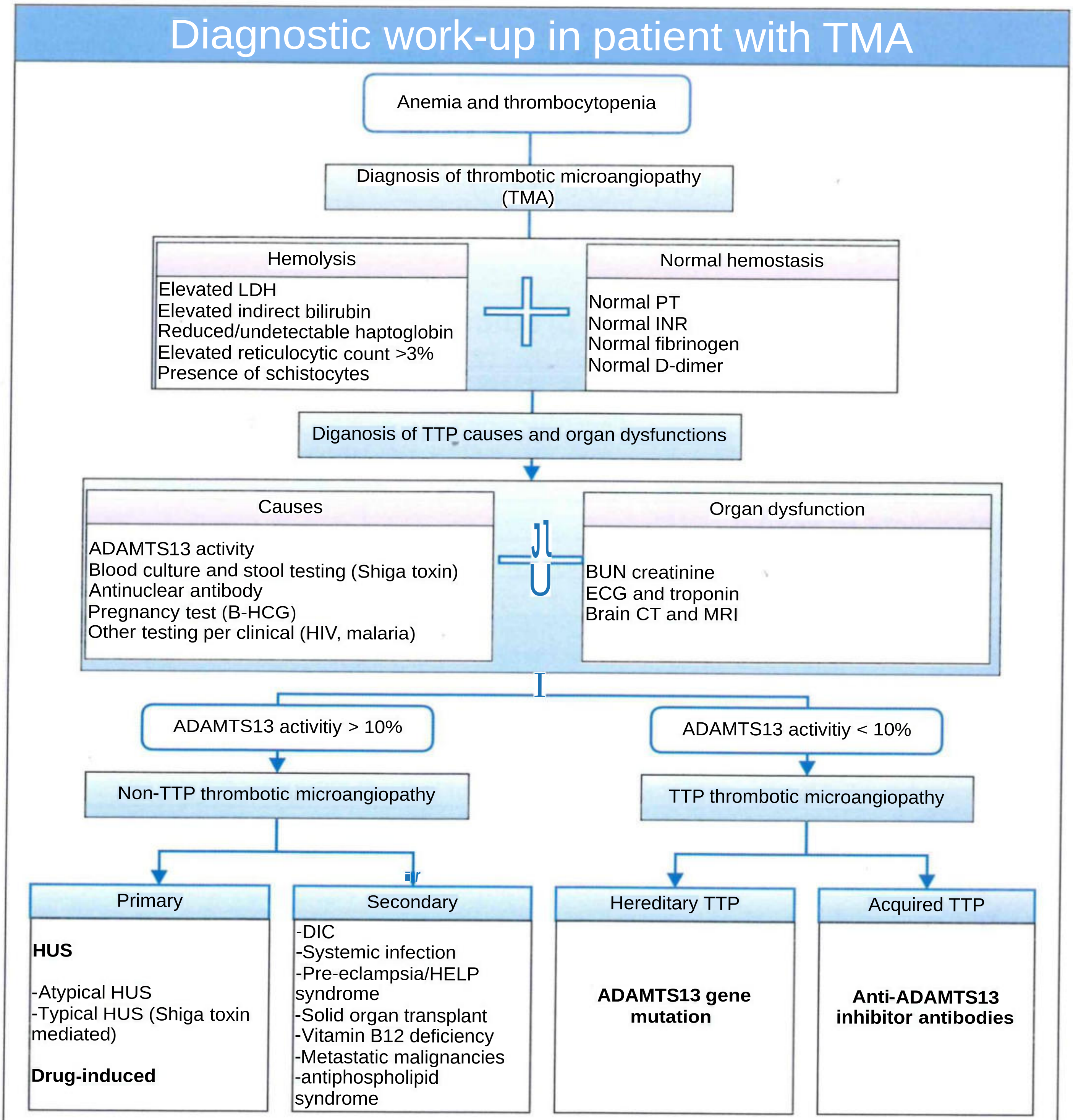
- Thrombotic thrombocytopenic purpura (TTP) usually refers to the disorder of thrombotic microangiopathy (TMA) which include thrombocytopenia, hemolysis with schistocytes on blood smears, renal dysfunction and neurologic abnormalities
- The initial management focuses on ruling out other causes of TMA, namely, Shiga-toxin-related hemolytic uremic syndrome (HUS), complement-mediated HUS, and secondary TMA syndromes

Diagnostic workup TTP

- The diagnosis of TTP is based on clinical and laboratory findings
- An ADAMTS13 assay showing activity below 10% is diagnostic for TTP
- The ADAMTS13 activity assay is not yet widely available and several scoring systems such as PLASMIC score have therefore been developed to predict severe ADAMTS13 deficiency and a diagnosis of TTP. (Table 39 -4)
- Diagnostic workup in patient with thrombotic microangiopathy Is described in Figure 39 -3

Table 39-4: PLASMIC score for predicting severe ADAMTS13 deficiency.

PLASMIC score		
Criteria	Points	Probability of severe ADAMTS13 deficiency
Platelets count < 30 X109/L	**1**	≤4 low
Combined hemolysis variables *	**1**	
No active malignancy	1	5-6 intermediate
No history of transplantation	1	
MCV < 90 fL	1	6-7 risk > 80%
INR < 1.5	1	
Creatinine < 2 mg/dl	**1**	
* Reticulocytes > 2–5% or undetectable haptoglobin or indirect bilirubin > 2.0 mg/dL		


Diagnostic work-up in patient with TMA
Anemia and thrombocytopenia
Diagnosis of thrombotic microangiopathy (TMA)
Hemolysis
Elevated LDH
Elevated indirect bilirubin
Reduced/undetectable haptoglobin
Elevated reticulocytic count >3%
Presence of schistocytes
Normal hemostasis
Normal PT
Normal INR
Normal fibrinogen
Normal D-dimer
Diganosis of TTP causes and organ dysfunctions
Causes
ADAMTS13 activity
Blood culture and stool testing (Shiga toxin)
Antinuclear antibody
Pregnancy test (B-HCG)
Other testing per clinical (HIV, malaria)
Organ dysfunction
BUN creatinine
ECG and troponin
Brain CT and MRI
ADAMTS13 activitiy > 10%
ADAMTS13 activitiy < 10%
Non-TTP thrombotic microangiopathy
TTP thrombotic microangiopathy
Primary
HUS
-Atypical HUS
-Typical HUS (Shiga toxin mediated)
Drug-induced
Secondary
-DIC
-Systemic infection
-Pre-eclampsia/HELP syndrome
-Solid organ transplant
-Vitamin B12 deficiency
-Metastatic malignancies
-antiphospholipid syndrome
Hereditary TTP
ADAMTS13 gene mutation
Acquired TTP
Anti-ADAMTS13 inhibitor antibodies

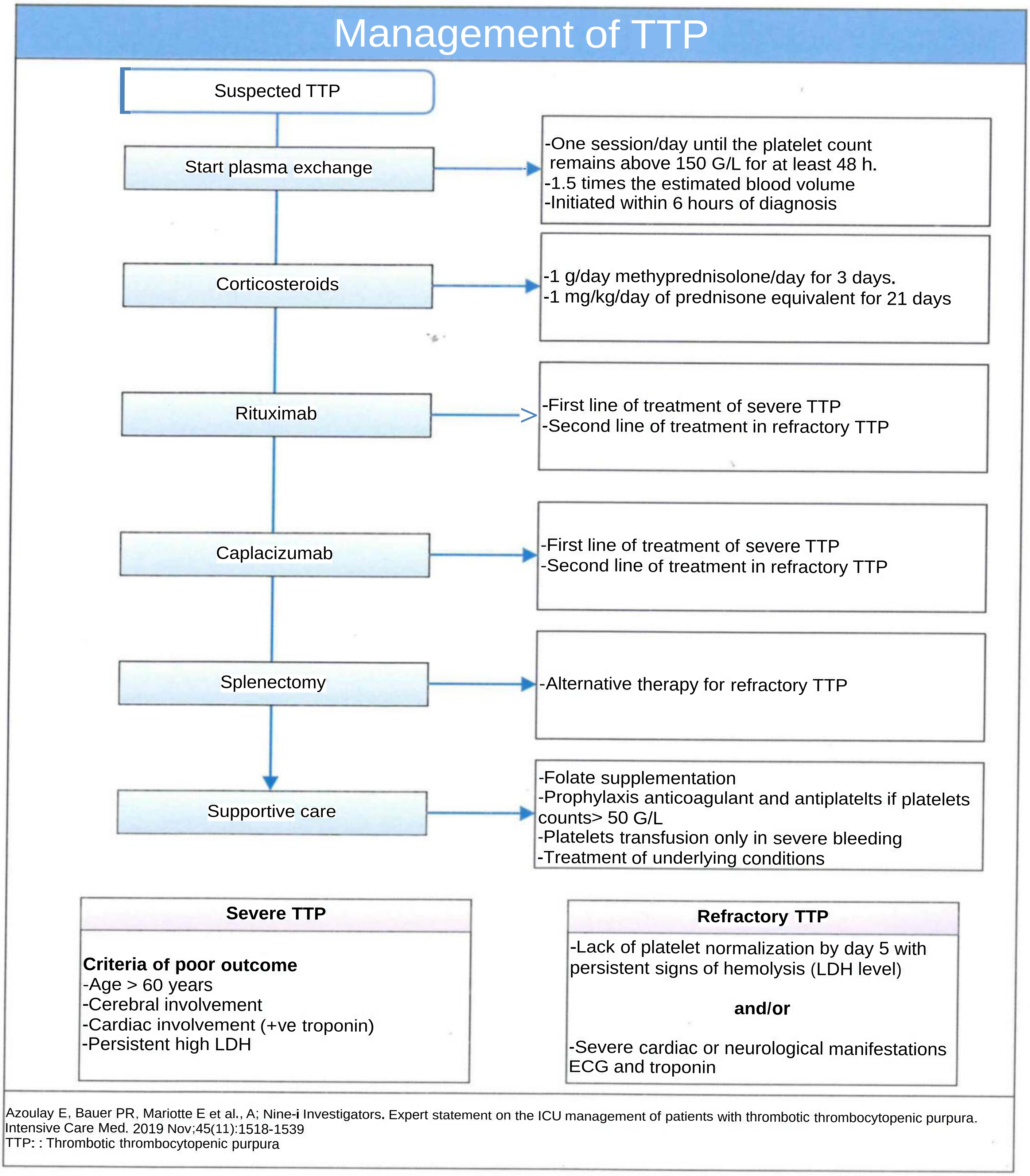
Azoulay E, Bauer PR, Mariotte E, A; Nirte-i Investigators. Expert statement on the ICU management of patients with thrombotic thrombocytopenic purpura. Intensive Care Med. 2019 Nov;45(11):1518-1539

TMA: : Thrombotic microangiopathy, DIC: disslminated intravascular coagulopathy, HELP: hemolysis elevated liver enzyme, low platelet count. HUS: hemolytic uremic syndrome

Figure 39-3: Diagnostic workup in patient with thrombotic microangiopathy

Management

- Management of TTP is described in Figure 39-4



Management of TTP

Suspected TTP

Start plasma exchange
-One session/day until the platelet count remains above 150 G/L for at least 48 h.
-1.5 times the estimated blood volume
-Initiated within 6 hours of diagnosis

Corticosteroids
-1 g/day methyprednisolone/day for 3 days.
-1 mg/kg/day of prednisone equivalent for 21 days

Rituximab
-First line of treatment of severe TTP
-Second line of treatment in refractory TTP

Caplacizumab
-First line of treatment of severe TTP
-Second line of treatment in refractory TTP

Splenectomy
-Alternative therapy for refractory TTP

Supportive care
-Folate supplementation
-Prophylaxis anticoagulant and antiplatelts if platelets counts> 50 G/L
-Platelets transfusion only in severe bleeding
-Treatment of underlying conditions

Severe TTP
Criteria of poor outcome -Age > 60 years -Cerebral involvement -Cardiac involvement (+ve troponin) -Persistent high LDH

Refractory TTP
-Lack of platelet normalization by day 5 with persistent signs of hemolysis (LDH level) **and/or** -Severe cardiac or neurological manifestations ECG and troponin

Azoulay E, Bauer PR, Mariotte E et al., A; Nine-i Investigators. Expert statement on the ICU management of patients with thrombotic thrombocytopenic purpura. Intensive Care Med. 2019 Nov;45(11):1518-1539
TTP: : Thrombotic thrombocytopenic purpura

Figure 39-4: TTP management

References

1. Azoulay E, Bauer PR, Mariotte E et al., A; Nine-i Investigators. Expert statement on the ICU management of patients with thrombotic thrombocytopenic purpura. Intensive Care Med. 2019 Nov;45(11):1518-1539

Chapter 40

Coagulopathy in critically ill

General Principles

- Coagulation disorders are severe, frequent complications in critically ill patients
- Coagulopathy is a generic term that can be defined as any alteration or disturbance of hemostasis due to multiple causes that result in either bleeding, clotting, or both

Classification of coagulopathy

- Based on the dominant clinical phenotype, coagulopathy in critically ill patient can be classified into hemorrhagic coagulopathy and thrombotic coagulopathy

Hemorrhagic coagulopathies

Non-malignant hemorrhagic coagulopathies

- Trauma-induced and peripartum induced coagulopathy
- Bleeding at the site is causing hypocoagulable state with activation of fibrinolysis
- Hemorrhagic coagulopathy is further worsened by uncontrolled bleeding and hemodilution

Malignant hemorrhagic coagulopathies

- Leukemia and pancreatic cancer
- Tumor cells express tissue factors that leads coagulation activation that is largely overwhelmed with hyperfibrinolysis

Thrombotic coagulopathies

Sepsis-induced coagulopathy

- Sepsis-induced coagulopathy is dysfunctional systemic activation of the coagulation cascade leading to excess thrombotic and hemorrhagic complications resulting from intravascular fibrin formation, microangiopathic thrombosis, and subsequent depletion of coagulation factors and platelets.
- Coagulopathy in septic patients progresses from an initially compensated derangement of the hemostatic system, termed sepsis-induced coagulopathy (SIC) non-overt DIC, to overt disseminated intravascular coagulopathy (DIC), a totally decompensated coagulation state.

Solid cancer-associated coagulopathy

- Unlike sepsis-induced DIC, patients display minimal clinical symptoms, with mild/ sub-acute/ chronic clinical manifestations of platelet and coagulation factor consumption

Diagnosis:

- Take history of known systemic conditions associated with coagulation disorders
- Laboratory investigations:
  - Complete blood count
  - Prothrombin time (PT), partial thromboplastin time (PTT), INR
  - Fibrinogen level, fibrin degradation product (FDP), D-dimer.
  - Renal and liver function tests.

- The commonest abnormality is thrombocytopenia followed by elevated FDPs, prolonged PT, prolonged PTT, and a low fibrinogen.
- Calculate SIC and DIC score of International Society of Thrombosis and Hemostasis
- (ISTH).
    - » SIC score ≥ 4 is suggestive for SIC (non-over DIC]
    - » DIC score ≥ 5 is suggestive for overt DIC
- Diagnostic score for SIC and DIC is described in Table 40-1
- Interpretation of laboratory results is described in Table 40 -2

Table 40-1: : International society on thrombosis and hemostasis criteria for DIC and SIC diagnosis

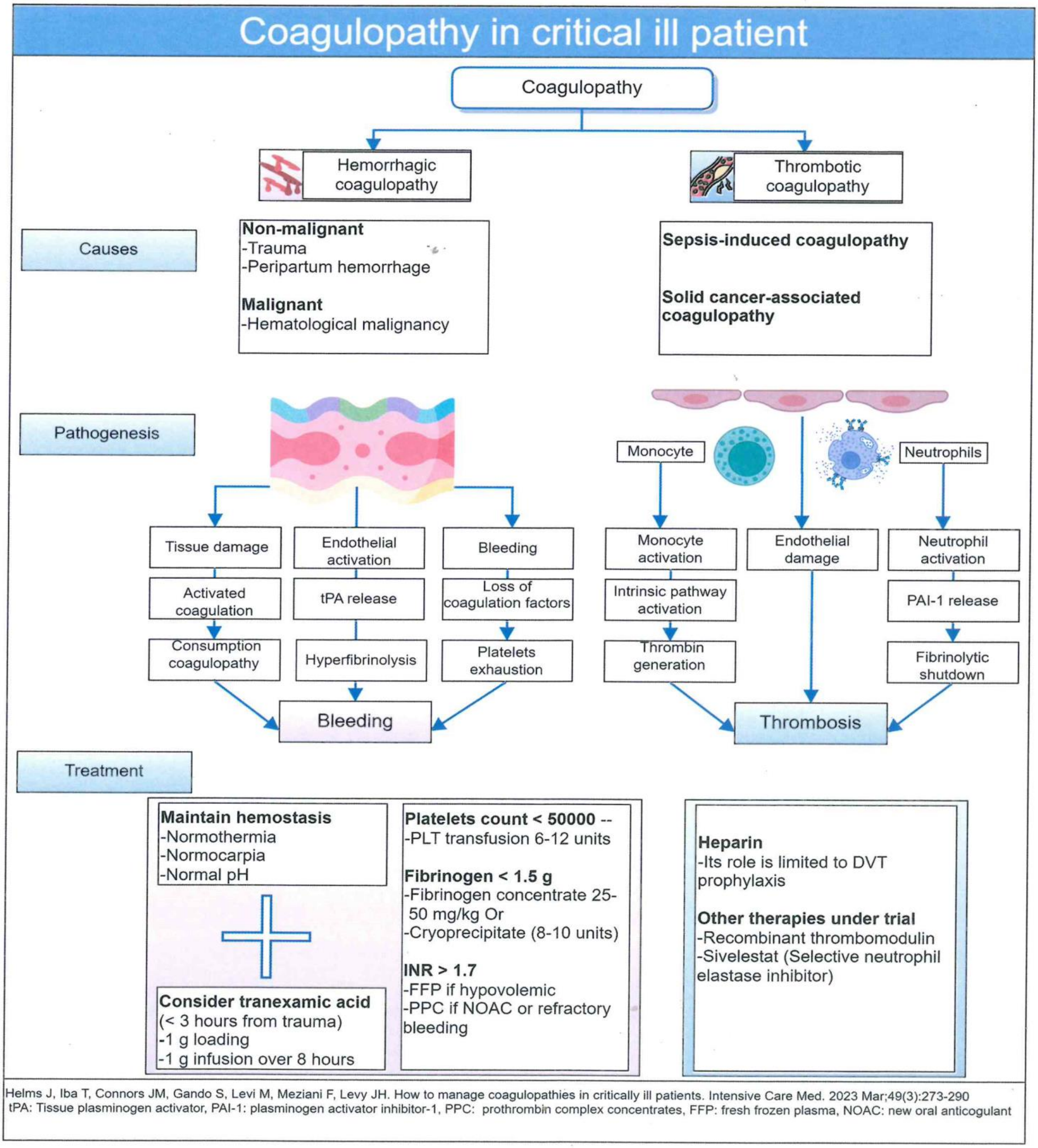
Item	Score	SIC	Overt DIC
Platelet Count (X109/ L)	2	**<100**	<50
	1	≥100, < 150	≥50, < 100
D-Dimer	3	---	>4000 ng/ml
	2	---	400-4000 ng/ml
INR	2	>1.4	>1.7
	1	**(1.2-1.4]**	(1.3-1.73
Fibrinogen g/dL	1	---	**<100**
SOFA score	2	≥2	---
	1	>1	---
Total score for SIC or DIC		≥4	≥5

Table 40-2: interpretation of laboratory results

Test results	Causes
PT prolonged aPTT normal	• Factor VII deficiency • Mild vitamin K deficiency • Mild liver insufficiency • Low dose vitamin K antagonists
PT normal aPTT prolonged	• Factor VIII, IX, XI deficiency • Unfractionated heparin • Anti- phospholipid antibody
PT prolonged aPTT prolonged	• Factor X, V, II or fibrinogen deficiency • Severe vitamin K deficiency • Vitamin K antagonists • Global clotting factor deficiency » Synthesis liver failure » Loss massive hemorrhage » Consumption DIC

Management

- Treatment of underlying cause.
- Transfusion of platelets or plasma (components) in patients with coagulopathy should not primarily be based on laboratory results and should in general be reserved for patients that present with bleeding (Figure 40-1)


Coagulopathy in critical ill patient
Coagulopathy
Hemorrhagic coagulopathy
Thrombotic coagulopathy
Causes
Non-malignant
-Trauma
-Peripartum hemorrhage
Malignant
-Hematological malignancy
Sepsis-induced coagulopathy
Solid cancer-associated coagulopathy
Pathogenesis
Tissue damage
Activated coagulation
Consumption coagulopathy
Endothelial activation
tPA release
Hyperfibrinolysis
Bleeding
Loss of coagulation factors
Platelets exhaustion
Bleeding
Monocyte
Neutrophils
Monocyte activation
Intrinsic pathway activation
Thrombin generation
Endothelial damage
Neutrophil activation
PAI-1 release
Fibrinolytic shutdown
Thrombosis
Treatment
Maintain hemostasis
-Normothermia
-Normocarpia
-Normal pH
Consider tranexamic acid
(< 3 hours from trauma)
-1 g loading
-1 g infusion over 8 hours
Platelets count < 50000 --
-PLT transfusion 6-12 units
Fibrinogen < 1.5 g
-Fibrinogen concentrate 25-50 mg/kg Or
-Cryoprecipitate (8-10 units)
INR > 1.7
-FFP if hypovolemic
-PPC if NOAC or refractory bleeding
Heparin
-Its role is limited to DVT prophylaxis
Other therapies under trial
-Recombinant thrombomodulin
-Sivelestat (Selective neutrophil elastase inhibitor)

Helms J, Iba T, Connors JM, Gando S, Levi M, Meziani F, Levy JH. How to manage coagulopathies in critically ill patients. Intensive Care Med. 2023 Mar;49(3):273-290
tPA: Tissue plasminogen activator, PAI-1: plasminogen activator inhibitor-1, PPC: prothrombin complex concentrates, FFP: fresh frozen plasma, NOAC: new oral anticoagulant

Figure 40-1: Pathogenesis and management of coagulopathy in critically ill patient

References

1. Helms J, Iba T, Connors JM, Gando S, Levi M, Meziani F, Levy JH. How to manage coagulopathies in critically ill patients. Intensive Care Med. 2023; 49:273-290
2. Tsantes AG, Parastatidou S, Tsantes EA, et al. Sepsis-Induced Coagulopathy: An Update on Pathophysiology, Biomarkers, and Current Guidelines. Life (Basel). 2023;13:350

Chapter 41

Anemia

General Principles

- Anemia is highly prevalent among the critically ill; 60% of patients admitted to intensive care units (ICU) are anaemic and 20–30% have a first hemoglobin concentration (Hb) <9.0 g/dL
- After 7 d, 80% of ICU patients have an Hb <9.0 g/dL and 30–50% of ICU patients receive red cell (RBC) transfusions
- Anemia is caused by several factors:
  - » Iron deficiency
  - » Bleeding
  - » Infection
  - » Cancer
  - » Chemotherapy
  - » Medication
  - » Reduced erythropoietin production
  - » Hemolysis

Diagnosis of anemia

- Complete blood picture
- Reticulocyte count
- Bilirubin, LDH and haptoglobin in patient with high reties
- Coomb's test to exclude hemolytic anemia.
- Ferritin and transferrin saturation
- Serum creatinine and TSH
- Diagnostic workup is described in Figure 41 -1

Management of anemia in critically ill patient

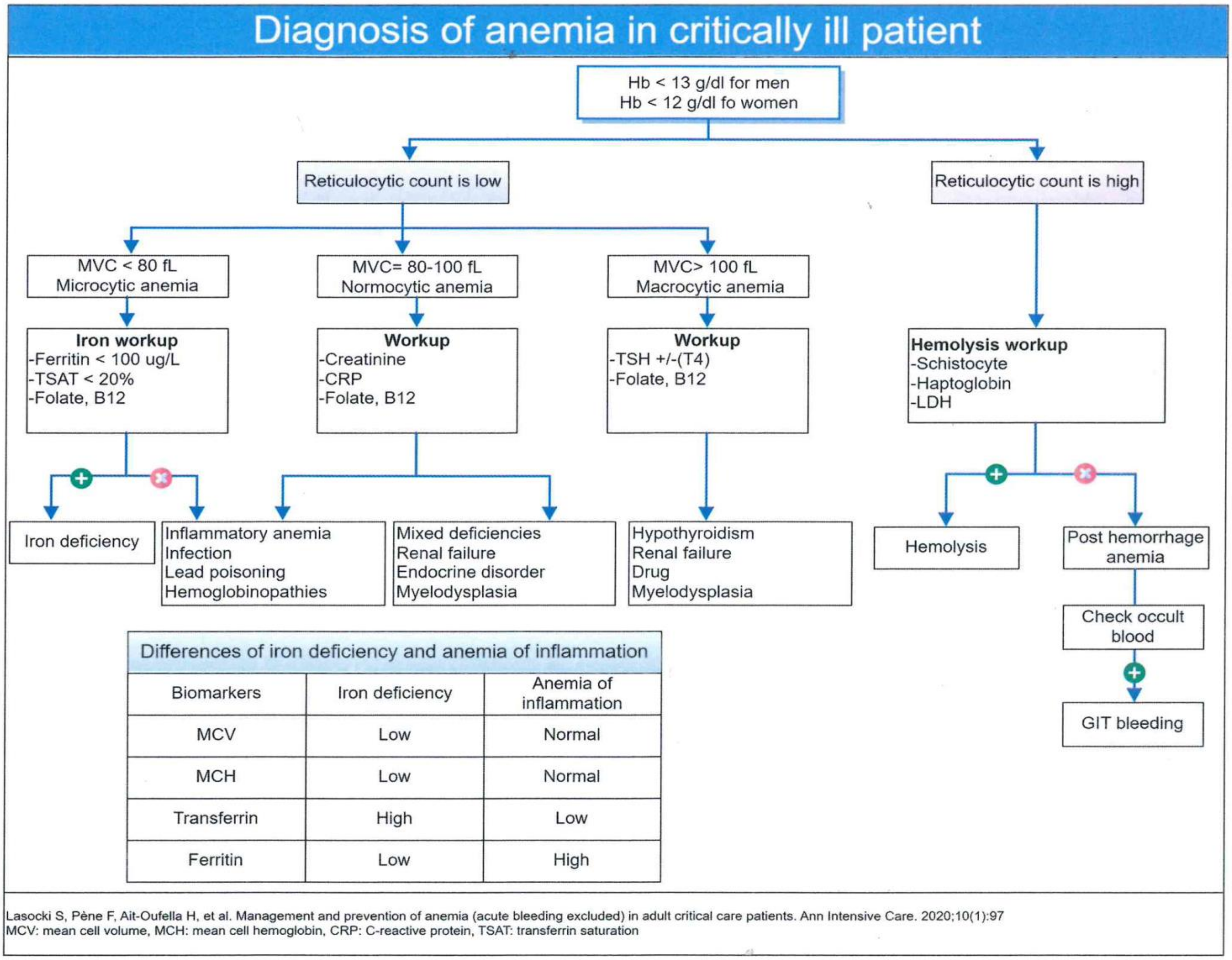
Transfusion trigger

- Transfusion is indicated for patients with acute bleeding and hemodynamic instability or evidence of inadequate oxygen delivery, as demonstrated by elevated lactic acid or base deficit.
- In non-bleeding patient, transfusion trigger of 7.0 g/dL or below, with a target Hb range of 7.0–9.0 g/dL, should be the default for all critically ill patients
- It is recommended to transfuse single unit of red blood cells followed by review of the indication for subsequent transfusion in order to reduce red blood cell utilisation
- Transfusion target should not exceed 9.0 g/dL in most critically ill patients.
- In patients with brain injuries and acute coronary syndrome, transfusion target should not exceed 10 g/dl

- Evidence for transfusion in patients with subarachnoid hemorrhage should be individualized
- Blood transfusion trigger in different population is illustrated in Figure 41 -2

Use of erythropoiesis-stimulating agent

- Erythropoiesis-stimulating agents are reommended to be used in critically ill anemic (Hb ≤ 10.0–12.0 g/dL) and/or trauma patients in the absence of contraindication.
- The recommended dose is 40,000 IU by subcutaneous injection once weekly in combination with an iron supplement
- It is not recommended to administer iron to reduce red blood cell utilisation or morbidity and mortality in critical care patients, except in combination with erythropoiesis-stimulating agents.
- Conversion between Epoetin alpha and Darbepoetin alpha is described in Figure 41 -2

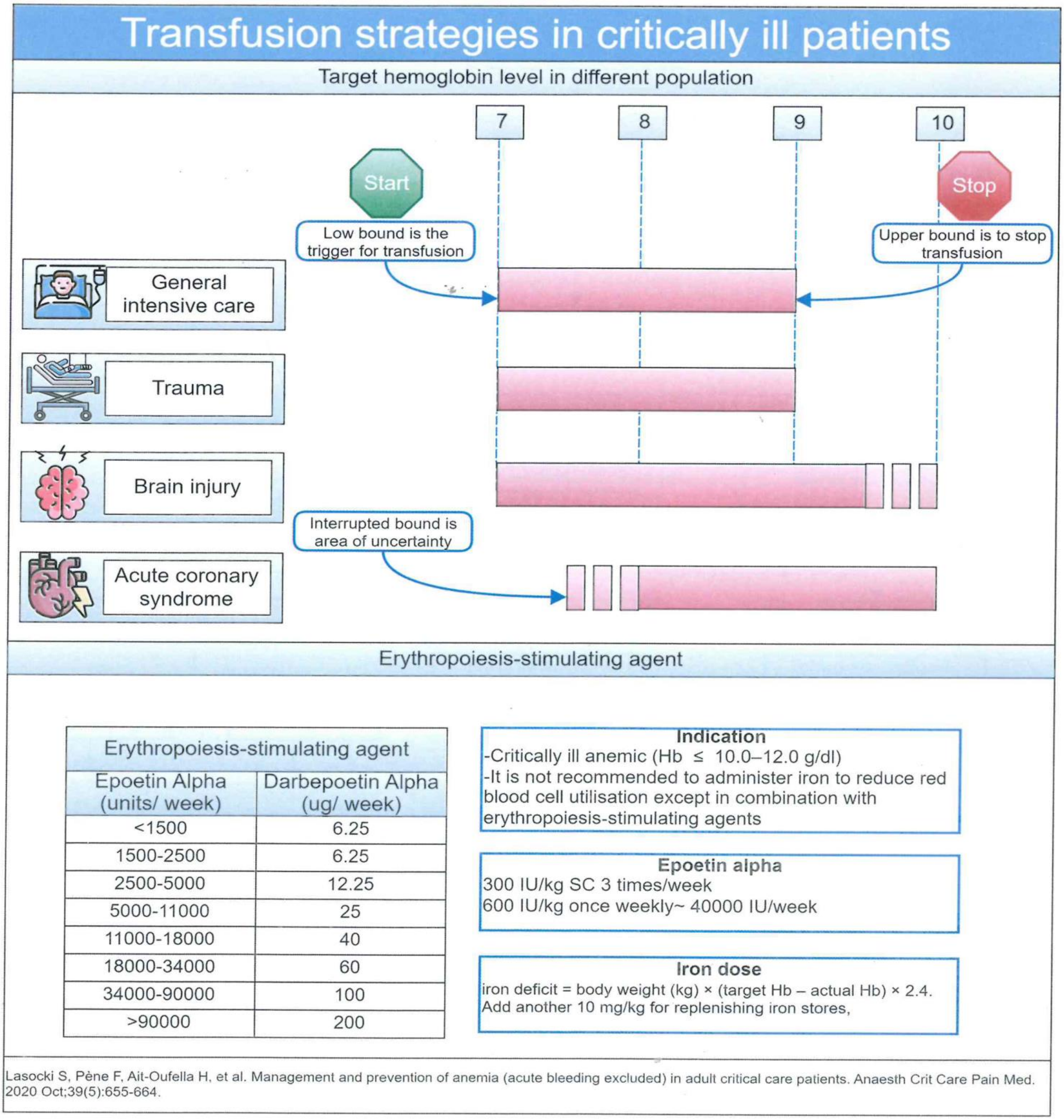

Diagnosis of anemia in critically ill patient
Hb < 13 g/dl for men
Hb < 12 g/dl fo women
Reticulocytic count is low
Reticulocytic count is high
MVC < 80 fL
Microcytic anemia
MVC= 80-100 fL
Normocytic anemia
MVC> 100 fL
Macrocytic anemia
Iron workup
-Ferritin < 100 ug/L
-TSAT < 20%
-Folate, B12
Workup
-Creatinine
-CRP
-Folate, B12
Workup
-TSH +/-(T4)
-Folate, B12
Hemolysis workup
-Schistocyte
-Haptoglobin
-LDH
+
×
Iron deficiency
Inflammatory anemia
Infection
Lead poisoning
Hemoglobinopathies
Mixed deficiencies
Renal failure
Endocrine disorder
Myelodysplasia
Hypothyroidism
Renal failure
Drug
Myelodysplasia
+
×
Hemolysis
Post hemorrhage anemia
Check occult blood
+
GIT bleeding

Differences of iron deficiency and anemia of inflammation

Biomarkers	Iron deficiency	Anemia of inflammation
MCV	Low	Normal
MCH	Low	Normal
Transferrin	High	Low
Ferritin	Low	High

Lasocki S, Pène F, Ait-Oufella H, et al. Management and prevention of anemia (acute bleeding excluded) in adult critical care patients. Ann Intensive Care. 2020;10(1):97
MCV: mean cell volume, MCH: mean cell hemoglobin, CRP: C-reactive protein, TSAT: transferrin saturation

Figure 41-1: Diagnosis of anemia in critically ill patient



Transfusion strategies in critically ill patients
Target hemoglobin level in different population
7
8
9
10
Start
Low bound is the trigger for transfusion
Stop
Upper bound is to stop transfusion
General intensive care
Trauma
Brain injury
Interrupted bound is area of uncertainty
Acute coronary syndrome
Erythropoiesis-stimulating agent

Erythropoiesis-stimulating agent	
Epoetin Alpha (units/ week)	Darbepoetin Alpha (ug/ week)
<1500	6.25
1500-2500	6.25
2500-5000	12.25
5000-11000	25
11000-18000	40
18000-34000	60
34000-90000	100
>90000	200

Indication

-Critically ill anemic (Hb ≤ 10.0–12.0 g/dl)

-It is not recommended to administer iron to reduce red blood cell utilisation except in combination with erythropoiesis-stimulating agents

Epoetin alpha

300 IU/kg SC 3 times/week

600 IU/kg once weekly~ 40000 IU/week

Iron dose

iron deficit = body weight (kg) × (target Hb – actual Hb) × 2.4.

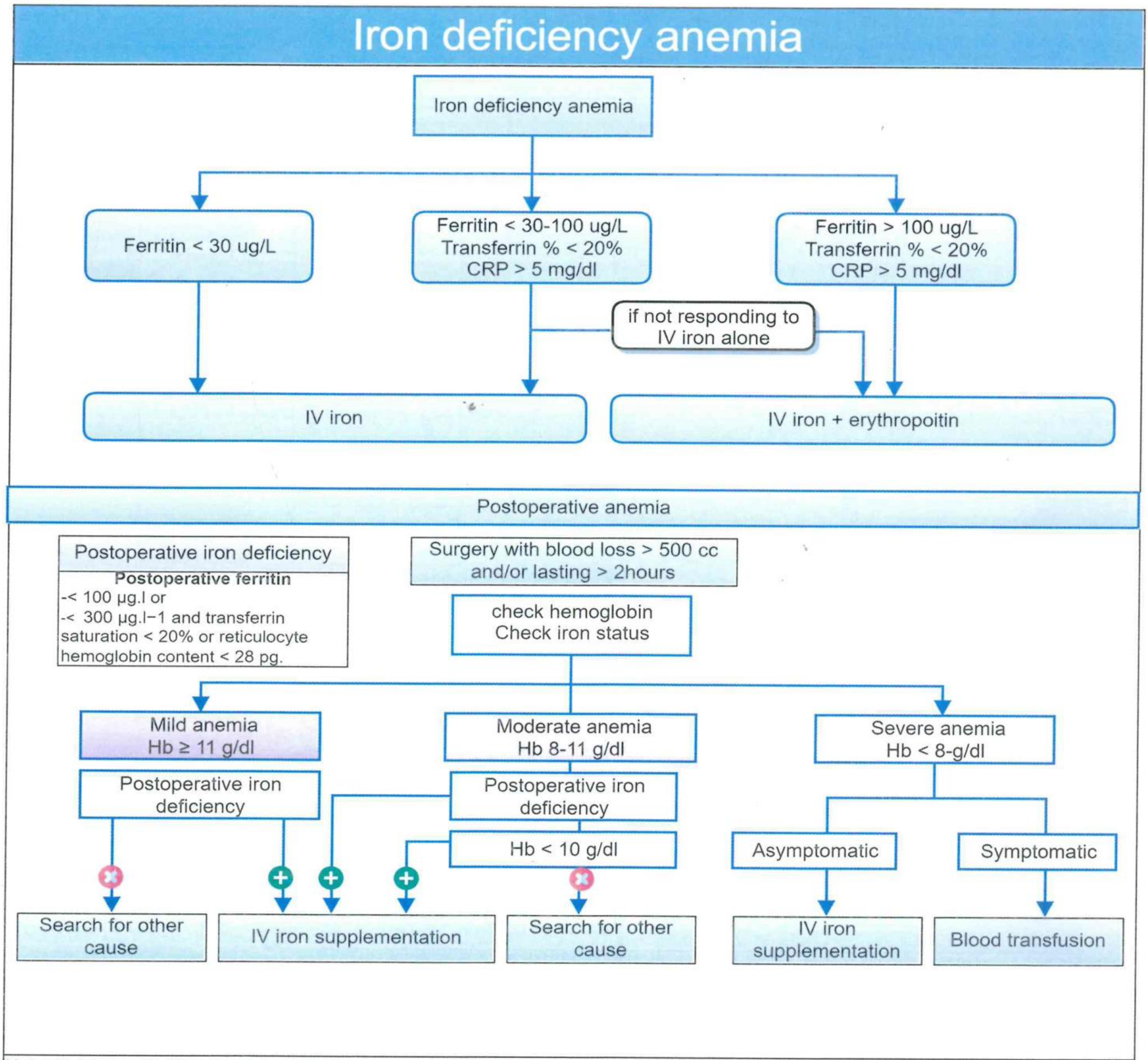
Add another 10 mg/kg for replenishing iron stores,

Lasocki S, Pène F, Ait-Oufella H, et al. Management and prevention of anemia (acute bleeding excluded) in adult critical care patients. Anaesth Crit Care Pain Med. 2020 Oct;39(5):655-664.

Figure 41-2: Transfusion trigger and doses of erythrpoiesis-stimualting agent

Diagnosis and treatment of Iron deficiency anemia

- Iron deficiency anemia management is described in Figure 41 -3


Iron deficiency anemia
Iron deficiency anemia
Ferritin < 30 ug/L
Ferritin < 30-100 ug/L
Transferrin % < 20%
CRP > 5 mg/dl
Ferritin > 100 ug/L
Transferrin % < 20%
CRP > 5 mg/dl
if not responding to IV iron alone
IV iron
IV iron + erythropoitin
Postoperative anemia
Postoperative iron deficiency
Postoperative ferritin
-< 100 μg.l or
-< 300 μg.l−1 and transferrin saturation < 20% or reticulocyte hemoglobin content < 28 pg.
Surgery with blood loss > 500 cc and/or lasting > 2hours
check hemoglobin
Check iron status
Mild anemia
Hb ≥ 11 g/dl
Moderate anemia
Hb 8-11 g/dl
Severe anemia
Hb < 8-g/dl
Postoperative iron deficiency
Postoperative iron deficiency
Hb < 10 g/dl
Asymptomatic
Symptomatic
Search for other cause
IV iron supplementation
Search for other cause
IV iron supplementation
Blood transfusion

Muñoz M, Acheson AG, Bisbe E,et al. An international consensus statement on the management of postoperative anemia after major surgical procedures. Anaesthesia. 2018;73:1418-1431.

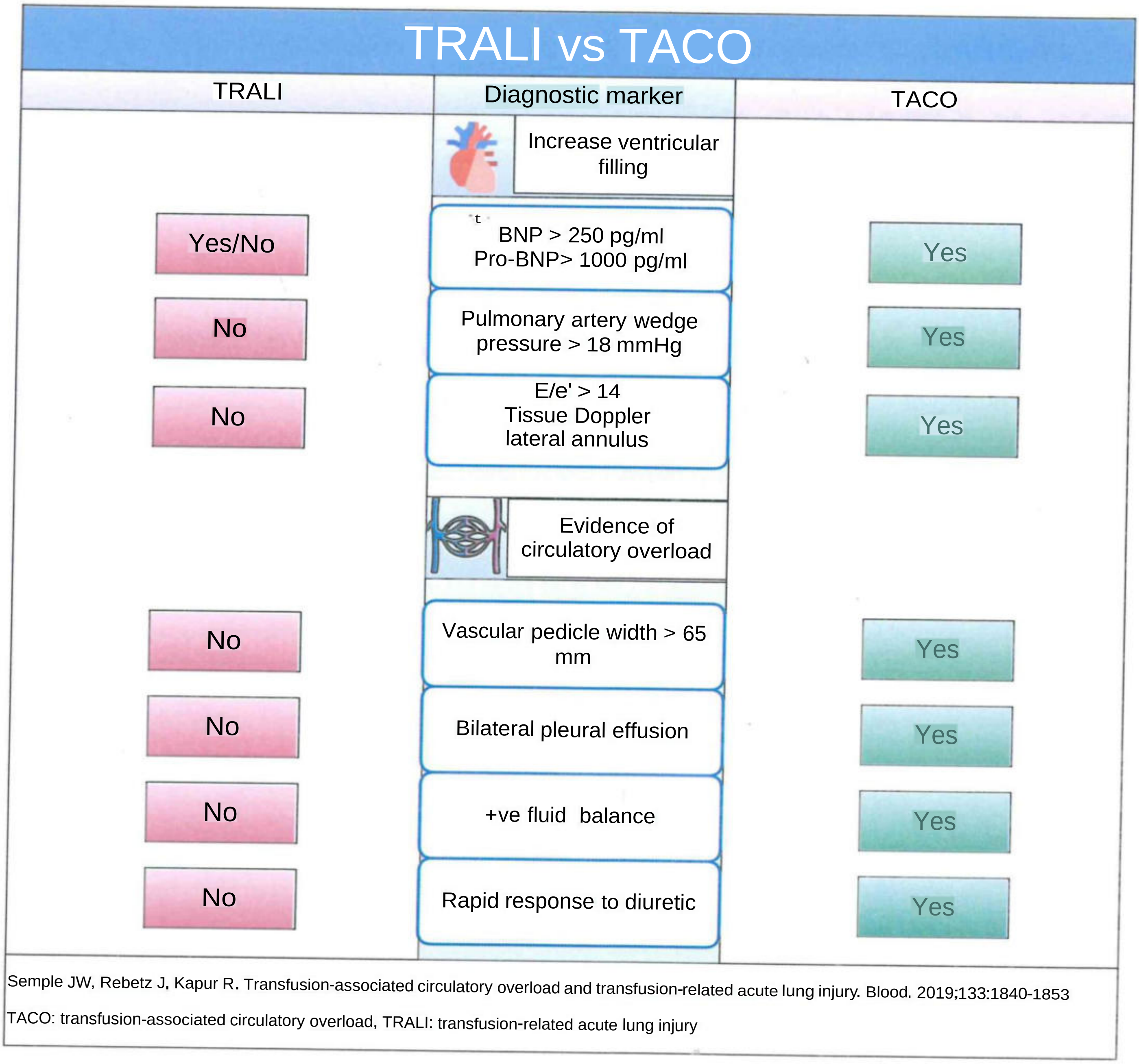
Figure 41-3: Management of iron deficiency anemia

Transfusion-related acute lung injury (TRALI)

- TRALI is defined as new acute lung injury (ALI) that occurs during or within six hours of transfusion, not explained by another ALI risk factor
- TRALI is subdivided into TRALI type I and TRALI type II. Table 41-1
- TRALI should be differentiated form transfusion-associated circulatory overload TACO. Clinical definition of TACO is similar to TRALI but may include evidence of positive fluid balance or cardiogenic involvement.
- The difference between TACO and TRALI is illustrated in Figure 41-4

Table 41-1: TRALI defintion

TRALI Type I
Patients who have no risk factors for ARDS and meet the following criteria: a. i. Acute onset ii. Hypoxemia (P/F ≤ 300 * or $SpO_2 < 90\%$ on room air) iii. Clear evidence of bilateral pulmonary edema on imaging iv. No evidence of left atrial hypertension (LAH) or, if LAH is present, it is judged to not be the main contributor to the hypoxemia b. Onset during or within 6 hr of transfusion c. No temporal relationship to an alternative risk factor for ARDS
TRALI Type II
Patients who have risk factors for ARDS (but who have not been diagnosed with ARDS) or who have existing mild ARDS (P/F of 200-300), but whose respiratory status worsens and is judged to be due to transfusion based on a. Findings as described in categories a and b of TRALI Type I, **And** b. Stable respiratory status in the 12 hr before transfusion



TRALI vs TACO

TRALI	Diagnostic marker	TACO
	Increase ventricular filling	
Yes/No	BNP > 250 pg/ml Pro-BNP> 1000 pg/ml	Yes
No	Pulmonary artery wedge pressure > 18 mmHg	Yes
No	E/e' > 14 Tissue Doppler lateral annulus	Yes
	Evidence of circulatory overload	
No	Vascular pedicle width > 65 mm	Yes
No	Bilateral pleural effusion	Yes
No	+ve fluid balance	Yes
No	Rapid response to diuretic	Yes

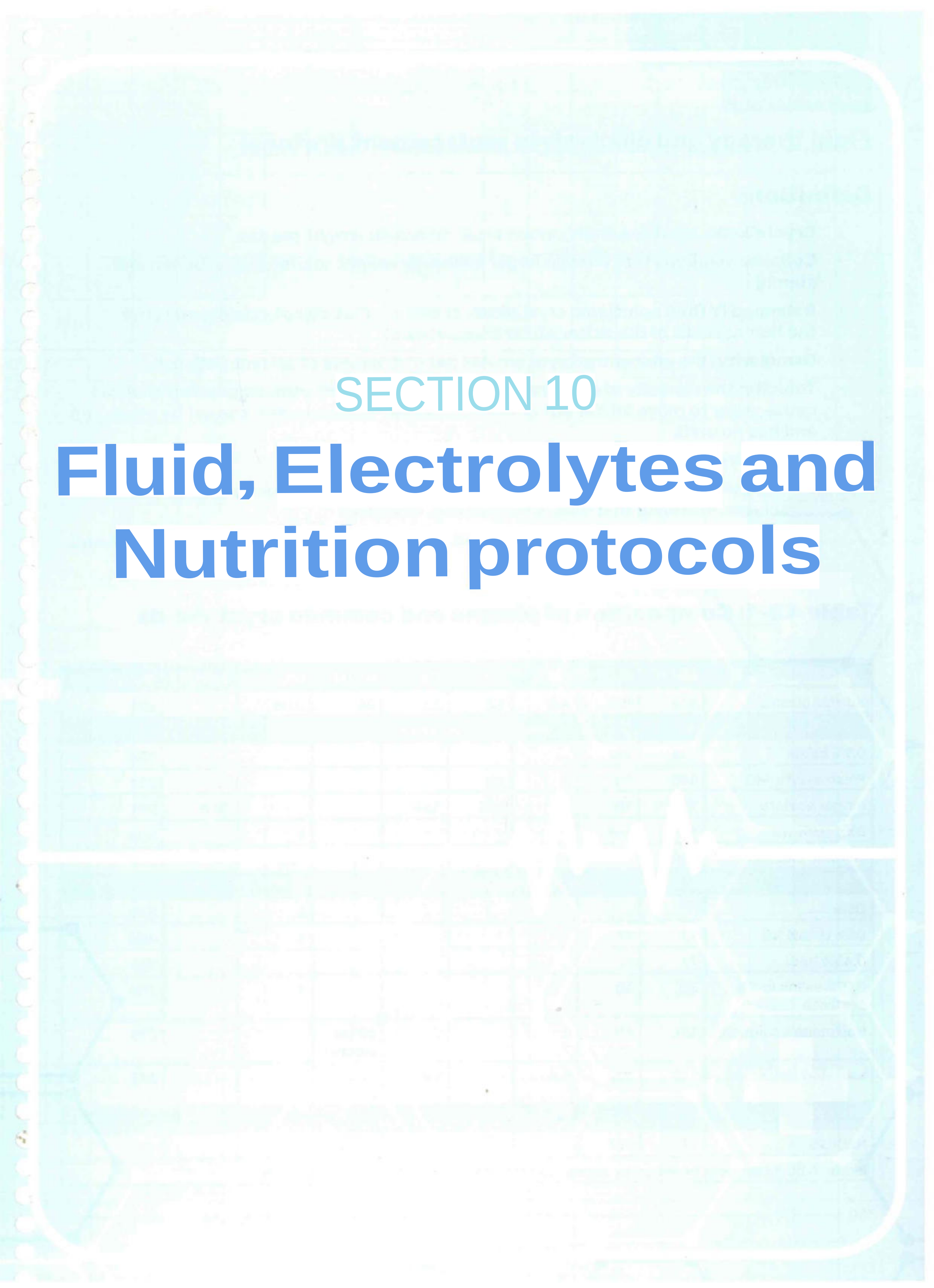
Semple JW, Rebetz J, Kapur R. Transfusion-associated circulatory overload and transfusion-related acute lung injury. Blood. 2019;133:1840-1853

TACO: transfusion-associated circulatory overload, TRALI: transfusion-related acute lung injury

Figure 41-4: Diagnostic features between TACO and TRALI

References

1. Lasocki S, Pene F, Ait-Oufella H, et al. Management and prevention of anemia (acute bleeding excluded) in adult critical care patients. Anaesth Crit Care Pain Med. 2020 39:655-664.
2. Munoz M, Acheson AG, Bisbe E, et al. An international consensus statement on the management of postoperative anaemia after major surgical procedures. Anaesthesia. 2018;73:1418-1431



SECTION 10

Fluid, Electrolytes and Nutrition protocols

SECTION 10

Chapter 42

Fluid therapy and electrolyte replacement protocol

Definitions

- **Crystalloids:** solutions that contain small molecular weight solutes
- **Colloids:** solutions that contain larger molecular weight solutes (e.g., albumin and starch)
- **Balanced IV fluid solutions:** crystalloids or colloids that do not significantly alter the homeostasis of the extracellular compartment.
- **Osmolarity:** the concentration of solutes per unit volume of solvent (mOsm/L)
- **Tonicity:** the capacity of an extracellular fluid to create an osmotic gradient that will cause water to move into or out pf the intracellular compartment; cannot be measured and has no units
- Osmolarity and tonicity are not the same.
  - » The osmolarity of parental solution takes into account the concentration of all solutes, including that enters the cell (e.g. dextrose)
  - » The tonicity of a solution is determined by the solutes that do not enter the cell and are, therefore, osmotically active.

Table 42-1: Composition of plasma and common crystalloids

Fluid	Na	Cl	K	Mg	Ca	HC03	Glucose	Acetate	Osmolarity
Normal plasma	142	103	4.5	1.2	2.5	24	0|08		291
Isotonic crystalloids									
0.9% saline	154	154							308
Plasma-Lyte 148	140	98	5	1.5				27	294
Ringer acetate	137	**112**	4	1.25	1.65			36.8	291
D5% 0.9% NS	154	154					5		506
Isotonic bicarbonate*	150					150	42.5		514
Hypotonic crystalloids									
D5%							5		278
D5% 0.45% NS	77	77					5		406
0.45% NaCl	77	77							154
0.18% saline in 4% dextrose	30	30					4		284
Hartmann's solution	131	**111**	5		**2**	29 (as lactate)			278
Lactated Ringer's	131	109	5.4		**1.8**	28 (as lactate)			273
Hypertonic crystalloids									
NaCl 3%	513	513							11027

Isotonic bicarbonate is prepared by adding 150 mL of 8.4% NaHC03 to 850 mL of D5%

Types of fluids used in critically ill patients

Resuscitation fluids

- In general, crystalloids that contain sodium in the range 130-154 mmol/l, with a bolus of 500 ml over 15-30 minutes are used in resuscitation.
- The types of fluid may differs according to indication of resuscitation as follow

Sepsis

- Saline or balanced crystalloids are used in patient with septic shock
- Hydroxyethyl starches SHOULD NOT be used in patient with sepsis
- Albumin in addition to crystalloids for volume replacement in patients with sepsis and septic shock when patients require substantial amounts of crystalloids

Traumatic Hypovolemic shock

- Isotonic or balanced crystalloid solutions are recommended in the hypotensive bleeding trauma patient.
- Excessive use of 0.9% NaCl solution should be avoided.

Traumatic brain injury

- Normal saline
- Hypotonic solutions such as Ringer's Lactate should be avoided in patients with severe head trauma
- Albumin should be avoided in patient with TBI

Liver cirrhosis and acute kidney injury

- Albumin 20% should be used in patient with AKI and suspected hypovolemia

Burn

- Lactated Ringer is used for Parkland formula

pH-guided resuscitation

Non-anion gap metabolic acidosis

- Isotonic bicarbonate 1.3%
- Isotonic bicarbonate is generally formulated by adding 150 mEq of sodium bicarbonate to a liter of D5%

Metabolic alkalosis

- Normal saline 0.9%

Maintenance Fluids

- Maintenance fluid should cover the daily requirement which include
  - » 25-30 ml/kg/day of water and
  - » Approximately 1 mmol/kg/day of potassium, sodium and chloride and
  - » Approximately 50-100 g/day of glucose to limit starvation ketosis.
- Type of fluid: D5% 0.2%NS with added 40mmol/l potassium. Alternatively, a mixture of 5% glucose and 0.9% sodium chloride bags in a ratio of two bags of 5% glucose to one of 0.9% sodium chloride

Replacement fluids

- Relacement fluid is required to replace ongoing external fluid losses, such as those caused by diarrhea and vomiting, gastrointestinal fistula, polyuric phase of acute renal failure, and excessive sweating.
- Types of replacement fluid differs according to the types of losses.
  - Polyuria and excessive sweating should be replaced by increase the rate of maintenance hypotonic fluid.
  - Gastrointestinal losses such as pancreatic fistula, biliary drainage, and high output ileal fistula is rich of sodium chloride and should be replaced by balanced solution e.g Lactated Ringer.
- A guide for types of replacement fluid is described in Table 42-2

Table 42-2: Guidelines for Replacement of Fluid Losses from the Gastrointestinal Tract

	Replace mL Per mL with	Add
Gastric (vomiting or nasogastric aspiration)	0.45% NaCl	KCl, 10 meq/L
Small bowel	0.45% NaCl	KCl, 10 meq/L
Biliary	Ringer Lactate or acetate	
Large bowel (diarrhea)	0.45 NaCl	KCl, 20 meq/L
Urine	0.45% NaCl	KCl, 10 meq/L

Electrolyte Replacement Protocol:

- Patients must meet the following criteria prior to initiation of the potassium, magnesium, or phosphorus protocols:
  - SCr < 2 mg/dL
  - Weight > 40kg

Hypokalemia

- Normal potassium levels: 3.6 – 5.5 meEq/L
- Hypokalemia classifications
  - Mild: 3.0 – 3.5 meEq/L
  - Moderate: 2.5 – 3.0 meEq/L
  - Severe: < 2.5 meEq/L

Potassium replacement protoc

- Recommended rate of infusion is 10 mEq/h
- Maximum rate of intravenous replacement is 20 mEq/h with continuous ECG monitoring (the maximum rate may be increased to 40mEq/h in emergency situations
- Maximum concentration for central IV administration= 20 mEq/50mL
- Maximum concentration for peripheral IV administration = 10 mEq/50 mL
- Potassium replacement therapy is described in Table 42 -3

Table 42-3: Potassium replacement protocol

Current Serum Potassium Level	Treatment	Recheck
3.3 – 3.9 mEq/L	40 mEq IV/PO	With next morning lab
3.0 – 3.2 mEq/L	60 mEq IV/PO	With next morning lab
2.6 – 2.9 mEq/L	80 mEq IV	Immediately and with next morning labs
< 2.6 mEq/L	100 mEq IV	Immediately and with next morning labs

Hypomagnesemia

- Normal magnesium levels: 1.7 – 2.5 mg/dL
- Hypomagnesemia classifications
  - » Mild: 1.5 – 1.9 mg/dL
  - » Moderate: 1.0 – 1.5 mg/dL
  - » Severe: < 1.0 mg/dL

Magnesium replacement protocol:

- Infusions should be no faster than 1gm of magnesium sulfaté over 30-60 minutes.
- Standard concentrations: 1 gm/100 mL and 2 gm/50 mL
- Conversion factor: 1 mmol= 2 mEq=24 mg of elemental magnesium=240 mg magnesium sulphate
- Magnesium replacement therapy is described in Table 42 -4

Table 42-4: Magnesium replacement protocol

Current Serum magnesium Level	Treatment	Recheck
1.5-1.9 mg/dL	IV 1 to 2 g over 1- 2 hours	With next morning lab
1.0 – 1.5 mg/dL	IV 2 to 4 g over 2- 12 hours	Within 6 hours of completing dose
< 1.0 mg/dL	IV 4 to 8 g over 4- 24 hours	Within 6 hours of completing dose
Hemodynamically unstable (e.g Torsades de pointes)	IV 1 to 2 g over 2-15 minutes	Within 2 hours of completing dose

Hypophosphatemia

- Normal phosphate levels: 2.8 – 4.5 mg/dL
- Hypophosphatemia classifications
  - » Mild: 2.0 – 2.5 mg/dL
  - » Moderate: 1.0 – 2.0 mg/dL
  - » Severe: < 1.0 mg/dL

Phosphate replacement protocol:

- Common phosphate products and their specific electrolytes concentrations is illustrated in Table 42 -5
- Maximum infusion rate
  - » Central line 15 mmol phos/hr
  - » Peripheral line -6.5 phos/hr

- Always look at potassium level to determine appropriate IV product
  - If K < 4 mEq/L use IV K-Phos
  - If K > 4 mEq/L use IV Na-Phos
- IV phosphate is potentially dangerous as it can precipitate with calcium and produce hypocalcemia and arrhythmia.
- Phosphate replacement therapy is described in Table 42 -6

Table 42-5: phosphate products

Product	Phosphate concentration	Potassium concentration	Sodium concentration
K-phosp neutral tab	250 mg (8 mmol)	1.1 mEq	13 mEq
K-phosp injection (per ml)	3 mmol	4..4 mEq	
Na-phos injection (per ml)	3 mmol		4 mEq

Table 42-6: Phosphate replacement protocol

Current Serum Phosphate Level	Treatment	Recheck
2.0-2.5 mg/dL	15 mmol IV k-phos or Na-phos Or Neutral tablet 2 tabs PO q4 x 3 doses	With next morning lab
1.6 - 1.9 mg/dL	30 mmol IV k-phos or Na-phos Or Neutral tablet 2 tabs PO q4 x 4 doses	Within 6 hours of completing dose
< 1.0 mg/dL	45 mmol IV k-phos or Na-phos	Within 6 hours of completing dose

Hypocalcemia

- Corrected total serum calcium level=measured total serum calcium +0.8 X (4-albumin level)

Table 42-7: Classification of hypocalcemia

Classification	Ionized	Total
Mild Mild	3.5 - 4.3 mg/dL	8 - 8.5 mg/dL
Moderate	2.5 - 3.4 mg/dL	7.5-8.0 mg/dL
Severe	< 2.5 mg/dL	<7.5 mg/dL

Calcium replacement protocol:

- Infuse at a rate of 2 grams/hour .
- Calcium chloride contains 3 times more elemental calcium than calcium gluconate.
- Calcium chloride must be administered through central line
  - Maximum rate 1 g IV over 10 min
- Calcium gluconate can be administered through central line or peripheral line
  - Maximum rate 3 g IV over 10 min
- Calcium replacement therapy is described in Table 42-8

Table 42-8: Calcium replacement protocol

Current Serum Phosphate Level	Treatment	Recheck
3.S-3.9 mg/dL	2 g IV calcium gluconate	With next morning lab
3.0 – 3.4 mg/dL	4 g IV calcium gluconate	Within 4 hours of completing dose
2.5-2.9 mg/dL	6 g IV calcium gluconate	Within 4 hours of completing dose
< 2.5 mg/dL	8 g IV calcium gluconate	Within 4 hours of completing dose

References

1. Frost P. Intravenous fluid therapy in adult inpatients. BMZJ. 2015 Dan 6;350:g7620
2. Finfer S. Myburgh 0, Bellomo R. Intravenous fluid therapy in critically ill adults. Nat Rev Nephrol. 2018; 14:541-557.

Chapter 43

Sodium imbalance

Hyponatremia:

Definitions

Biochemical defintion

- Definition of hyponatremia based on biochemical severity
  - » **Mild Hyponatremia:** serum sodium concentration between 130 and 135 mmol/l.
  - » **Moderate' Hyponatremia:** serum sodium concentration between 125 and 129 mmol/l.
  - » **Profound Hyponatremia:** serum sodium concentration <125 mmol/l.

Timing definition

- Definition of hyponatremia based on time of development:
  - » **Acute Hyponatremia:** hyponatremia that is documented to exist <48 h.
  - » **Chronic Hyponatremia:** hyponatremia that is documented to exist for at least 48 h.
  - » If hyponatremia cannot be classified, we consider it being chronic, unless there is clinical or anamnestic evidence of the contrary.

Symptomatic definition

- Definition of hyponatremia based on symptoms:
  - » **Moderately severe hyponatremia:** any biochemical degree of hyponatremia in the presence of moderately severe symptoms of hyponatremia
    - Nausea without vomiting
    - Confusion
    - Headache
  - » **Severe hyponatremia:** any biochemical degree of hyponatremia in the presence of severe symptoms of hyponatremia.
    - Vomiting
    - Cardiorespiratory distress
    - Seizures
    - Coma (Glasgow coma scale ≤ 8)

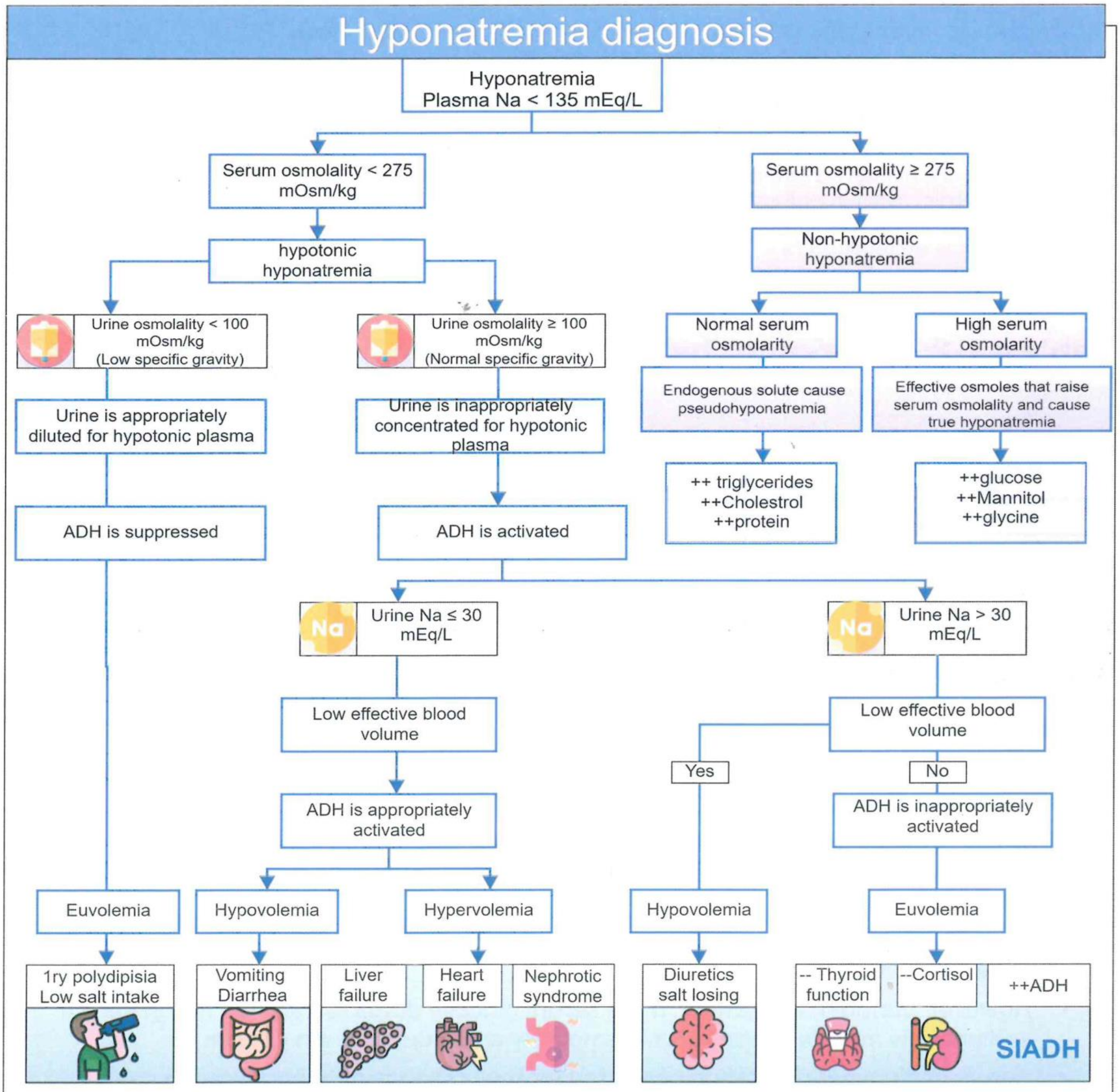
Etiological definition

- Definition of hyponatremia based on etiology
  - » **Non-hypotonic:** measured serum osmolality ≥ 275 mOsm/kg
    - **Pseudohyponatremia:** presence of endogenous solutes that cause lab error in measuring serum sodium e.g. high, triglycerides, proteins, cholesterols.
    - **True hyponatremia:** Presence of effective osmoles that raise serum osmolality and causes true hyponatremia

- Hypotonic hyponatremia: Measured serum osmolality < 275 mOsm/kg which is further classified according to volume status into
  - Hypovolemic
  - Euvolemic
  - Hypervolemic

Diagnosis of hyponatremia:

- Diagnosis of hyponatremia is a 3-step approach:
  - Measure serum osmolarity to differentiate hypotonic from non-hypotonic hyponatremia:
    - Serum osmolality is ≥ 275 mOsm/L -> non-hypotonic hyponatremia.
    - Serum osmolality is < 275 mOsm/L -> hypotonic hyponatremia.
  - Measure urine osmolality or specific gravity:
    - Urine osmolality is < 100 mOsm/L -> Low sodium intake or polydipsia
    - Urine osmolality is > 100 mOsm/L -> measure urinary sodium
  - Measure urinary sodium:
    - Urinary sodium < 30 mmol/L -> ADH is appropriately secreted
      - Hypovolemia -> vomiting, diarrhea
      - Hypervolemia -> liver failure, heart failure, or nephrotic syndrome
    - Urinary sodium ≥ 30 mmol/L -> check volume status:
      - Hypovolemia in diuretic use, salt losing nephropathy, or cerebral losing nephropathy.
      - Euvolemia in thyroid dysfunction, corticosteroid deficiency, or syndrome of inappropriate ADH (SIADH) secretion
        - Tyroid dysfunction is rarely to produce hyponatremia. serum sodium concentration decreased by 0.14 mmol/l for every 10 mU/l rise in thyroid-stimulating hormone. This indicates that only severe cases of clinically manifest hypothyroidism resulted in clinically important hyponatremia
- Diagnosis of hyponatremia is illustrated in Figure 43-1
- Diagnostic criteria for SIADH is described in Table 43-1
- Differential diagnosis between SIADH and cerebral salt losing syndrome is described in Table 43 -2


Hyponatremia diagnosis
Hyponatremia
Plasma Na < 135 mEq/L
Serum osmolality < 275 mOsm/kg
Serum osmolality ≥ 275 mOsm/kg
hypotonic hyponatremia
Non-hypotonic hyponatremia
Urine osmolality < 100 mOsm/kg (Low specific gravity)
Urine osmolality ≥ 100 mOsm/kg (Normal specific gravity)
Normal serum osmolarity
High serum osmolarity
Urine is appropriately diluted for hypotonic plasma
Urine is inappropriately concentrated for hypotonic plasma
Endogenous solute cause pseudohyponatremia
Effective osmoles that raise serum osmolality and cause true hyponatremia
++ triglycerides
++Cholestrol
++protein
++glucose
++Mannitol
++glycine
ADH is suppressed
ADH is activated
Na
Urine Na ≤ 30 mEq/L
Na
Urine Na > 30 mEq/L
Low effective blood volume
Low effective blood volume
Yes
No
ADH is appropriately activated
ADH is inappropriately activated
Euvolemia
Hypovolemia
Hypervolemia
Hypovolemia
Euvolemia
1ry polydipisia
Low salt intake
Vomiting
Diarrhea
Liver failure
Heart failure
Nephrotic syndrome
Diuretics
salt losing
-- Thyroid function
--Cortisol
++ADH
SIADH

pasovski G, Vanholder R, Allolio B, et al.. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Intensive Care Med. 2014;40:320-31.
SIADH: syndrome of inappropriate ADH

Figure 43-1: Diagnosis of hyponatremia

Table 43-1: Criteria for SIADH diagnosis

Essential criteria
• Effective serum osmolality <275 mOsm/kg • Urine osmolality >100 mOsm/kg • Clinical euvolemia • Urine sodium concentration >30 mmol/l with normal dietary salt and water intake • Absence of adrenal, thyroid, pituitary or renal insufficiency • No recent use of diuretic agents
Supplemental criteria
• Serum uric acid <0.24 mmol/l (<4 mg/dl) • Serum urea <3.6 mmol/l (<21.6 mg/dl) • Failure to correct hyponatremia after 0.9% saline infusion • Fractional sodium excretion >0.5% • Fractional urea excretion >55% • Fractional uric acid excretion >12% • Correction of hyponatremia through fluid restriction

Table 43-2: Differences between SIADH and cerebral salt wasting

	SIADH	Cerebral salt wasting
Serum urea	Normal-low	Normal-high
Serum uric acid	Low	Low
Urine volume	Normal-low	Normal-high
Blood pressure	Normal	Normal-othrostatic hypotension
Central venous pressure	Normal	Low

Treatment of hyponatremia:

Treatment of non-hypotonic hyponatremia

- Non-hypotonic hyponatremia does not cause brain edema and it is managed differently from hypotonic hyponatremia.
- When there are excess effective osmoles e.g glucose, it pulls the water from intracellular to extracellular compartment and this causes dilutional hyponatremia with no risk of brain edema.
- When the glucose is metabolized or excreted, the serum osmolarity decreases with rise of serum sodium.
- However, during management, if the serum glucose drops faster than rise of serum sodium, this may decrease serum osmolarity and induces brain edema.
- Serum sodium concentration corrected for the presence of hyperglycemia can be obtained from the following equation
    - » Corrected sodium= measured Na+ 2.4 X (glucose (mg/dl)-100)/100
- This translates into adding 2.4 mmol/l to the measured serum sodium concentration for every 5.5 mmol/l (100 mg/dl) incremental rise in serum glucose concentration above a standard serum glucose concentration of 5.5 mmol/l (100 mg/dl).
- To avoid brain edema during management of hyperglycemia, serum tonicity should be regularly measured using this equation

  - Tonicity=2x[Na]+[Glucose]mmol/L (1 mmol/L glucose= 18 mg/dl)
- The recommendation is to avoid decease in serum glucose by rate > 50-70 mg/dl or decline in tonicity at rate exceeding 3-8 mOsm/L/hr

Treatment of hypotonic hyponatremia

- Treatment of hyponatremia depends on whether symptoms is present or not and whether the hyponatremia is acute or chronic

Symptomatic hyponatremia

- In hyponatremia with severe symptoms,
  - Two boluses of hypertonic saline 3% should be given over 20 minutes to achieve increase of serum Na by 5 mmol/L
  - If the symptoms improve after the first 2 boluses,
    - hypertonic saline should be stopped
    - NaCl 0.9% should be started at lower rate till the complete the workup of hyponatremia.
    - Check serum Na after 6, 12 hrs and every 24 hrs afterward
    - Limit increase in serum Na to 10 mmol/L in 1st 24 hrs and an additional 8 mmol/l during every 24 hrs thereafter until the serum sodium concentration reaches 130 mmol/l
- If symptoms did not improve after first 2 boluses
  - Continue hypertonic saline 3% to increase Na by 1 mmol/l/hr
  - Change in the serum Na can be expected by Adrogue˙-Madias formula
    - Change in serum Na= Infusate(Na)-Serum (Na)/Total body water + 1
  - Saline infusion calculator in different body weights is described in Table 43 -3
  - Check serum Na every 4 hrs as long as an IV infusion of 3% is continued
  - Stop hypertonic saline if any of the following occur
    - Symptoms improve
    - Serum Na increases by 10 mmol/l
    - Serum Na reaches 130 mmol/L
- In hyponatremia with moderately-severe symptoms,
  - One bolus of hypertonic saline 3% should be given over 20 minutes to achieve increase of serum Na by 5 mmol/L
  - Check serum Na after 1, 6, and 12 hrs
  - Limit increase in serum Na to 10 mmol/L in 1st 24 hrs and an additional 8 mmol/l during every 24 hrs thereafter until the serum sodium concentration reaches 130 mmol/l

Table 43-3: Sodium rate calculator for correction of hyponatremia

Calculate total body water in liters					
Step 1	**wt in kg**	Men<65 yr	Men>65 or Woman<65 yr	Woman>65 yr	
	40	24	20	18	
	45	27	23	20	
	50	30	25	23	
	55	33	28	25	
	60	36	30	27	
	65	39	33	29	
	70	42	35	32	
	75	45	38	34	
	80	48	40	36	
	85	51	43	38	
	90	54	**45**	41	
	95	57	48	43	
	100	60	50	45	
	105	63	53	47	
	110	**66**	55	50	
	115	69	58	52	
	120	72	60	54	
	125	75	63	56	
	130	78	65	59	
	135	81	68	61	
	140	84	70	63	
	145	87	73	65	
	150	90	75	68	
	155	93	78	70	
	160	96	80	72	
	165	99	83	74	

Calculate Infusion Rate of Selected IV Fluids					
Step 2					
Maximum rate of IV infusion (ml/hr) for increase in Na of **0.5 mEq/L/hr**			Maximum rate of IV infusion (ml/hr) for increase in Na of **1 mEq/L/hr**		
TBW (Liters)	**0.9% Normal Saline**	**3% Saline**	**TBW (Liters)**	**0.9% Normal Saline**	**3% Saline**
20	65	19	**20**	130	39
25	81	24	**25**	162	49
30	97	29	**30**	195	58
35	114	34	**35**	227	**68**
40	130	39	**40**	260	78
45	146	44	**45**	292	**88**
50	162	49	**50**	325	97
55	179	54	**55**		107
60	195	58	**60**		117
65	**211**	63	**65**		127
70	227	68	**70**		136
75	244	73	**75**		147

Note: The infusion rates above are the maximum recommended rates to achieve the desired rate of Na increase. Initially, cap infusion rate of 3% saline at 75 mL/hour for a Na increase of 0.5 mEq/L/hour and at 150 mL/hr for an increase of 1mEq/L/hour.

TBW * (goal serum Na cone - current serum Na cone) / (IV fluid Na concentration/L) * 1000 (number of hours needed to correct Na).

Non-symptomatic hyponatremia

- In non-symptomatic hyponatremia, treatment depends on whether the hyponatremia is acute or chronic:
  - » Acute asymptomatic hyponatremia
    - Stop medication and fluids that provoke hyponatremia
    - If drop in serum Na > 10 mmol/L infuse 150 ml NaCl over 20 min
    - Check serum sodium after 4 hrs
- Chronic asymptomatic hyponatremia
  - » In moderate or profound hyponatremia, avoid an increase in serum sodium concentration of >10 mmol/l during the first 24 hrs and >8 mmol/l during every 24 hrs thereafter.
  - » Patients with reduced circulating volume (Hypovolemic hyponatremic)
    - restoring extracellular volume with i.v. infusion of 0.9% saline or a balanced crystalloid solution at 0.5-1.b ml/kg per hr
    - In case of hemodynamic instability, the need for rapid fluid resuscitation overrides the risk of an overly rapid increase in serum sodium concentration.
  - » Patients with expanded circulating volume (hypervolemic)
    - Fluid restriction
    - Loop diuretics
    - Start cause-specific treatment
    - Dialysis/ultrafiltration in refractory cases
  - » Patients with non-expanding circulating volume (Euvolemic)
    - Fluid restriction
    - Increase solute intake (0.2-0.5 g/kg urea)
    - combination of low-dose loop diuretics and oral sodium chloride
    - Vaptans and demeclocycline are controversials.
- Treatment of symptomatic hyponatremia is described in Figure 43 -2
- Treatment of chronic hyponatremia is described in Figure 43 -3

Overcorrection of hyponatremia

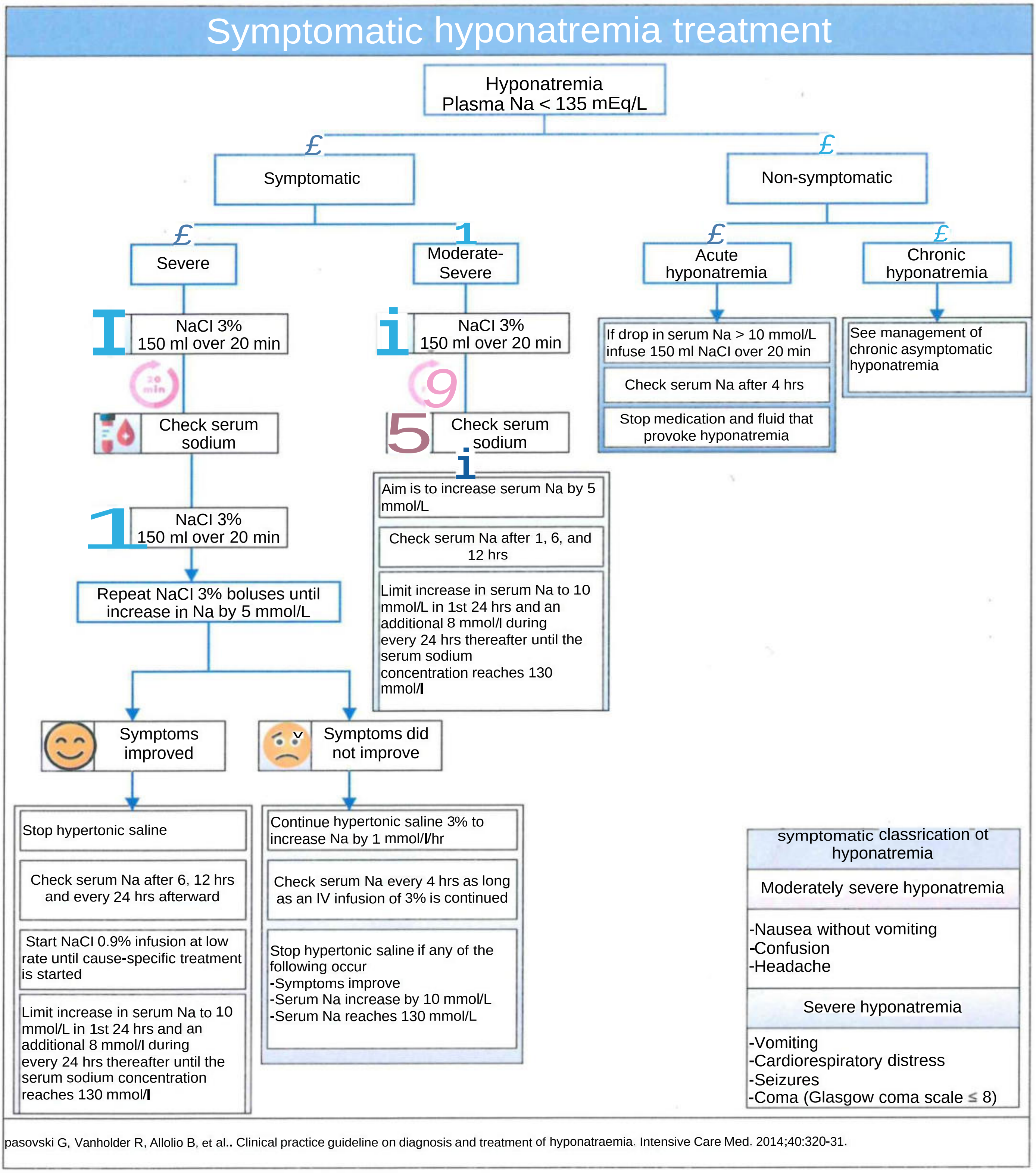
- Rapid correction of hyponatremia carries the risk of osmotic demylination (OD)
- Risk of OD is increased when the rate of Na correction exceeds 10 mmol/l in the first 24 hours and 18 mmol/l in 48 hours
- patients presenting with profound (<120 mmol/l) and chronic (>48 h) hyponatremia also carry a greater potential for OD
- Osmotic demylination affects pontine area (central pontine myelinolysis) and extra-pontine region mainly in cerebellum (Extra-pontine myelinolysis)
- Clinical signs of pontine and extra-pontine myelinolysis are described in Table 43-4
- Management of overcorrection of hyponatremia is described in Table 43 -5

Table 43-4: Clinical signs of osmotic demylination

Central pontine myelinolysis	Extra-pontine myelinolysis
Quadriparesis/plegia	Extra-pyramidal syndrome
Ataxia	Dystonia
Nystagmus	Choreoathetosis
Dysarthria	Myoclonus
Ophthalmoplegia	Opsoclonus
Dysphagia	Akinetic-rigid state
Pseudobulbar palsy	Akinetic mutism
Locked-in" syndrome	Emotional lability

Table 43-5: management of overcorrected hyponatremia

- Discontinuing the ongoing active treatment.
- Start an infusion of 10 ml/kg body weight of electrolyte-free water (e.g. glucose solutions) over 1 hr under strict monitoring of urine output and fluid balance.
- Add i.v. desmopressin 2 mg, with the understanding that this should not be repeated more frequently than every 8 hrs



Symptomatic hyponatremia treatment

Hyponatremia
Plasma Na < 135 mEq/L
Symptomatic
Non-symptomatic
Severe
Moderate-Severe
Acute hyponatremia
Chronic hyponatremia
NaCl 3% 150 ml over 20 min
20 min
Check serum sodium
NaCl 3% 150 ml over 20 min
Repeat NaCl 3% boluses until increase in Na by 5 mmol/L
Symptoms improved
Symptoms did not improve
NaCl 3% 150 ml over 20 min
Check serum sodium

Severe: Stop hypertonic saline

Check serum Na after 6, 12 hrs and every 24 hrs afterward

Start NaCl 0.9% infusion at low rate until cause-specific treatment is started

Limit increase in serum Na to 10 mmol/L in 1st 24 hrs and an additional 8 mmol/l during every 24 hrs thereafter until the serum sodium concentration reaches 130 mmol/l

Symptoms did not improve: Continue hypertonic saline 3% to increase Na by 1 mmol/l/hr

Check serum Na every 4 hrs as long as an IV infusion of 3% is continued

Stop hypertonic saline if any of the following occur
-Symptoms improve
-Serum Na increase by 10 mmol/L
-Serum Na reaches 130 mmol/L

Moderate-Severe: Aim is to increase serum Na by 5 mmol/L

Check serum Na after 1, 6, and 12 hrs

Limit increase in serum Na to 10 mmol/L in 1st 24 hrs and an additional 8 mmol/l during every 24 hrs thereafter until the serum sodium concentration reaches 130 mmol/l

Acute hyponatremia: If drop in serum Na > 10 mmol/L infuse 150 ml NaCl over 20 min

Check serum Na after 4 hrs

Stop medication and fluid that provoke hyponatremia

Chronic hyponatremia: See management of chronic asymptomatic hyponatremia

symptomatic classrication ot hyponatremia
Moderately severe hyponatremia
-Nausea without vomiting -Confusion -Headache
Severe hyponatremia
-Vomiting -Cardiorespiratory distress -Seizures -Coma (Glasgow coma scale ≤ 8)

pasovski G, Vanholder R, Allolio B, et al.. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Intensive Care Med. 2014;40:320-31.

Figure 43-2: Management of symptomatic hyponatremia

Hypernatremia:

- Hypernatremia is defined as serum Na level above 145 mmol/l
- It typically develops during ICU admission due to inadequate free water administration.
- Untreated hypernatremia is a hallmark of low-quality, ICU care.

Causes of Hypernatremia:

- The causes of hypernatremia in critically ill patients can be subdivided into 3 categories.
    - Water and solute deficit
    - Pure water deficit
    - Solute gain
- The most important cause of hypernatremia in critically ill patient is inadequate water intake.
- The differential diagnosis of hypernatremia depends on the assessment of extracellular fluid with and without assessment of urinary Na and K
- The different causes and differential diagnosis of hypernatremia are described in Figure 43 -4

Management of hypernatremia

Replacement of water deficit

- In the presence of hemodynamic instability with hypotension and hypernatremia, intravascular volume should be restored first with isotonic saline prior to free water administration.
- Correction of sodium requires replacement of free water deficit + daily fluid requirement and any ongoing losses
- Calculation of water deficit is derived from the following equation
    - Water Deficit=TBW X |Na[corrected]/Na[target]-1|
- Daily fluid requirement is calculated from urinary volume and urinary Na and K using this equation
    - Electrolyte free water=urinary volume X [1-Urinary Na + Urinary K/Serum Na]
- Correction of hypernatremia is illustrated in (Table 43-6)
- Rate of correction of hypernatremia should be done at a rate not exceeding 0.5 mEq/L per h to a total of 10 to 12 mEq/d.

Hypernatremia

	Water and solute deficit		Pure water deficit		Solute gain
Mechanisms	Renal loss	Extra-renal loss	Renal loss	Extra-renal loss	Excess sodium gain
	CT		§!		1
Causes	-loop diuretics -Osmotic diuretic -Post-obstruction -Acute and chronic kidney	-Fever -excercise -GIT loss -Burn	-Central DI -Nephrogenic DI	- Low water intake -Fever -mechanical ventilation	-Hypertonic saline -Sodium bicarbonate -mechanical ventilation -Correction of water loss with NaCl 0.9%
Lab findnig	-++ U-osmolality -U (Na+K)> P(Na)	-++ U-osmolality -U (Na+K)< P(Na)	- – U-osmolality -U (Na+K)< P(Na)	-++ U-osmolality -U (Na+K)> P(Na)	-++ U-osmolality -U (Na+K)< P(Na)
Treatment	Restore ECV with 0.9% NaCl if signs of hypoperfusion				Decrease NaCl input
	Restore water deficit				Increase sodium loss -Loop diuretics -Thiazide diuretics -Dialysis
	Treatment of the cause		Central DI: Desmopressin		
			Nephrogenic DI: Thiazide Low solute diet		

$$\text{Water deficit} = \text{TBW} \times \left[\frac{[\text{Na}^+]\ \textit{corrected}}{[\text{Na}^+]\ \textit{Target}} - 1 \right]$$

Water defecit

-Rate of correction should not exceed 12 mmol/l/day

-Daily fluid requirement should be replaced + calculated deficit

-Type of solution may be water PO, D5% or 0.45% Nacl IV

$$\text{Na } \textit{corrected} = \text{Measured Na} + 2.4 \times \left[\frac{\text{Glucose } (\textit{mg/dl}) - 100\ (\textit{mg/dl})}{100\ (\textit{mg/dl})} \right]$$

Overgaard-Steensen C, Ring T. Clinical review: practical approach to hyponatraemia and hypernatraemia in critically ill patients. Crit Care. 2013 ;17:206.
P(Na): plasma sodium, DI: diabetes insipidus, TBW: total body water, U(Na+K): Urinary sodium + potassium, ECV: Extracellular volume, D5%: dextrose 5%

Figure 43-4: Diagnosis and management of hypernatremia

Table 43-6: Correction of hypernatremia: working example

Example

Male patient 50-year old, weighing 70 kg. His sodium level is 150 mEq/L and blood glucose is 300 mg/dl. Total urine output in the past 24 hours is 2000 ml. Urinary sodium and potassium levels are 40 mEq/L

- Free Water deficit=TBW X [Na corrected/Na Target-1]
- Na corrected=Measured Na+2.4 X [Glucose mg/dl-100 mg/dl/100 mg/dl]
- Na corrected=150+2.4 X [300-100/100]=157 mg/dl
- Free water deficit=42 X [157/145-1]=3.47L
- Daily requirement=2000 X [1-40/157]=1.5L
- Total Fluid required=1.5+3.47= 5Liters
- Types of Fluid water PO V D596IV

Treatment of the cause

- Central diabetes insipidus
  - » DDAVP, an ADH analogue, can be administered orally, intranasally, subcutaneously, or intravenously.
  - » In adults, the dose is ten meg by nasal insufflation or 4mcg subcutaneously or intravenously.
- Nephrogenic diabetes insipidus
  - » The first step is to correct the underlying cause. discontinue the offending agent, such as lithium.
  - » Low solute diet
  - » Thiazide diuretics
  - » DDAVP and NSAIDs

References

1. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur D Endocrinol. 2014 25;170:G1-47
2. Overgaard-Steensen C, Ring T. Clinical review: practical approach to hyponatraemia and hypernatraemia in critically ill patients. Crit Care. 2013 ;17:206.

Chapter 44

High K, Ca, P04 serum level

Hyperkalemia:

- Hyperkalemia is defined as plasma level > 5.5 mmol/L and severe hyperkalemia as >6.5 mmol/L

Causes of hyperkalemia

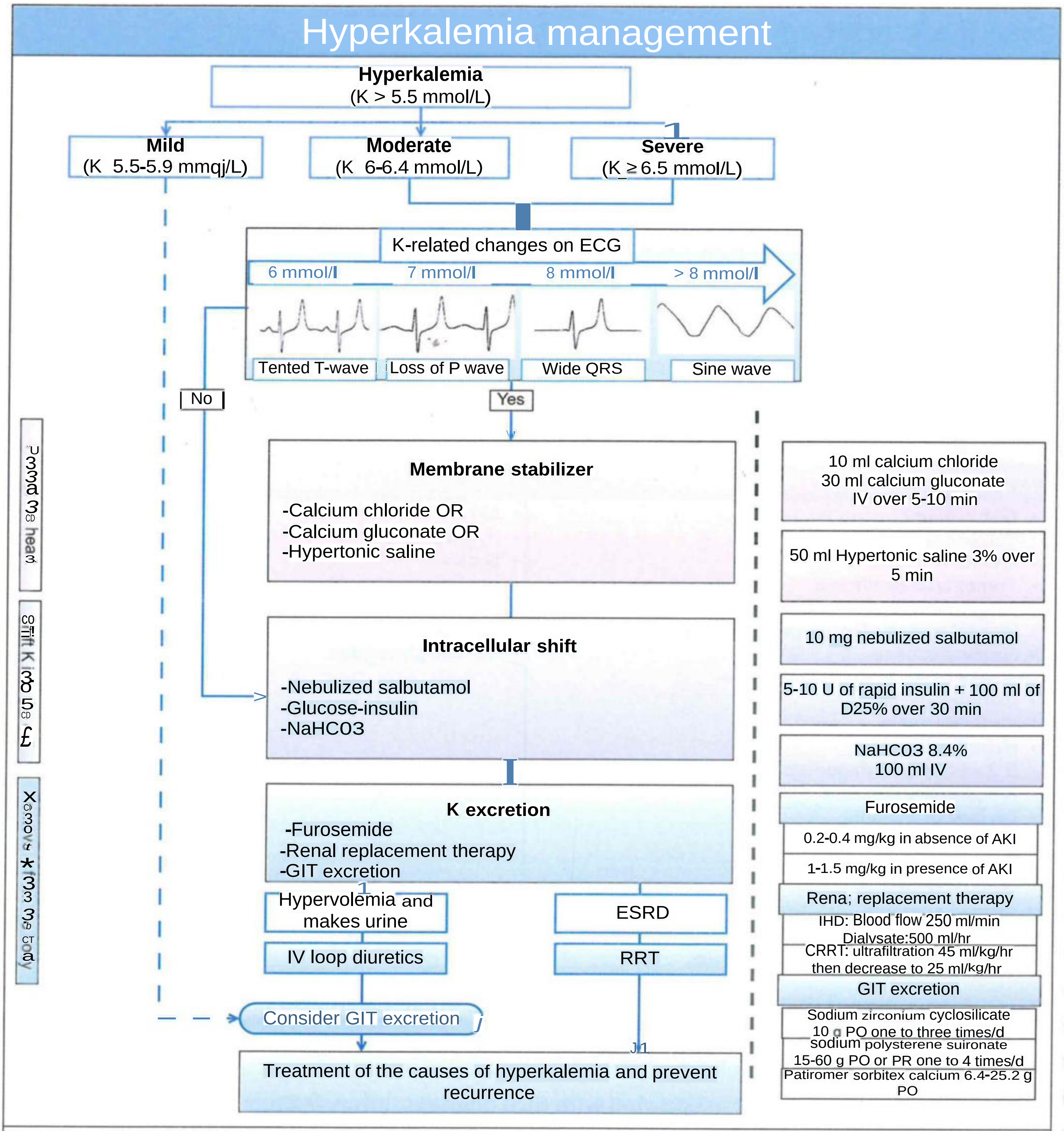
- Mechanisms contributing to hyperkalemia can be categorized into
  - Causes that increase extracellular potassium
  - Causes that decrease potassium elimination
- Causes of hyperkalemia is described in Table 44 -1

Table 44-1: Mechanism Contributing to the Development of Hyperkalemia

Increase extracellular K	Decrease K elimination
• Tissue injury • Hemolysis • Rhabdomyolysis • Tumor lysis syndrome **K+ shift in extracellular space** • Mineral acidosis (i.e., hyperchoride acidosis) • Succinylcholine **Inability to enter into myocyte** • Diabetes mellitus • Hyperglycemia • Hypertonicity • B 2 -receptor antagonists • Aldosterone blockers • Cardiac glycosides **High acute iatrogenic K+ load** • Increased dietary intake • Blood transfusion • Error of injection	• AKI • Hypovolemia • Sepsis • Acidosis treatment • RAAS inhibitor • Calcineurine inhibitor • Cardiac glycosides

Management of hyperkalemia:

- Management of hyperkalemia depends on the presence of ECG changes or not.
- If hyperkalemia is associated with ECG changes, drugs that acts on membrane stabilizers and intracellular shift should be administered
- If hyperkalemia is not associated with ECG changes, interventions that enhance k excretion should be initiated.
- K-related ECG changes and hyperkalemia management outline is described in Figure 44 -1
- The details of drugs dosage that are used in management of hyperkalemia is described in Figure 44 -2


Hyperkalemia management
Hyperkalemia
(K > 5.5 mmol/L)
Mild
(K 5.5-5.9 mmol/L)
Moderate
(K 6-6.4 mmol/L)
Severe
(K ≥ 6.5 mmol/L)
K-related changes on ECG
6 mmol/l
7 mmol/l
8 mmol/l
> 8 mmol/l
Tented T-wave
Loss of P wave
Wide QRS
Sine wave
No
Yes
Membrane stabilizer
-Calcium chloride OR
-Calcium gluconate OR
-Hypertonic saline
Intracellular shift
-Nebulized salbutamol
-Glucose-insulin
-NaHCO3
K excretion
-Furosemide
-Renal replacement therapy
-GIT excretion
Hypervolemia and makes urine
IV loop diuretics
ESRD
RRT
Consider GIT excretion
Treatment of the causes of hyperkalemia and prevent recurrence
10 ml calcium chloride
30 ml calcium gluconate
IV over 5-10 min
50 ml Hypertonic saline 3% over 5 min
10 mg nebulized salbutamol
5-10 U of rapid insulin + 100 ml of D25% over 30 min
NaHCO3 8.4%
100 ml IV
Furosemide
0.2-0.4 mg/kg in absence of AKI
1-1.5 mg/kg in presence of AKI
Renal replacement therapy
IHD: Blood flow 250 ml/min
Dialysate:500 ml/hr
CRRT: ultrafiltration 45 ml/kg/hr then decrease to 25 ml/kg/hr
GIT excretion
Sodium zirconium cyclosilicate
10 g PO one to three times/d
sodium polystyrene sulfonate
15-60 g PO or PR one to 4 times/d
Patiromer sorbitex calcium 6.4-25.2 g PO

Dépret F, Peacock WF, Liu KD, et al. Management of hyperkalemia in the acutely ill patient. Ann Intensive Care. 2019;9:32

IV: intravenous, PO: oral, PR: per-rectum, ESRD:End stage renal disease, RRT: renal replacement therapy, IHD: intermittent hemodialysis, CRRT: continuous renal replacement therapy, GIT:gastrointestinal

Figure 44-1: Management outline of hyperkalemia

Hypercalcemia

- **Hypercalcemia is defined as total serum Ca level above 10.5mg/dl or ionized serum Ca level above 5.6 mg/dl or 1.4 mmol/L**
- **Total serum Ca should be corrected for serum albumin using the fallowing equation**
  - **(4.0-Plasma serum albumin) (g/dl) X 0.8 + (serum calcium (mg/dl)**
- **Classification of hypercalcemia is described in Figure 44-3**

Causes of hypercalcemia

- **Causes of hypercalcemia can be categorized as parathormone-dependent causes and parathormone-independent causes.**
- **Causes of hypercalcemia are described in Table 44 -2**

Table 44-2: Causes of hypercalcemia

Parathyroid-dependent hypercalcemia	Parathyroid-independent hypercalcemia
Primary Hyperparathyroidism • Adenoma • Hyperplasia • Carcinoma (rare) Tertiary hyperparathyroidism Familial hypocalcuric hypercalcemia Lithium	Malignancy Local osteolitic osteolysis • Multiple bone metastasis • Diffuse marrow infiltration Humoral hypercalcemia of malignancy • Parathyroid hormone-related protein • 1,25 Dihydroxyvitamin D Granulomatous disease Hyperthyroidism Adrenal insufficiency Medications • Thiazide • Vitamin D • Calcium • Vitamin A • Teriparatide Immobilization

Symptoms of hypercalcemia

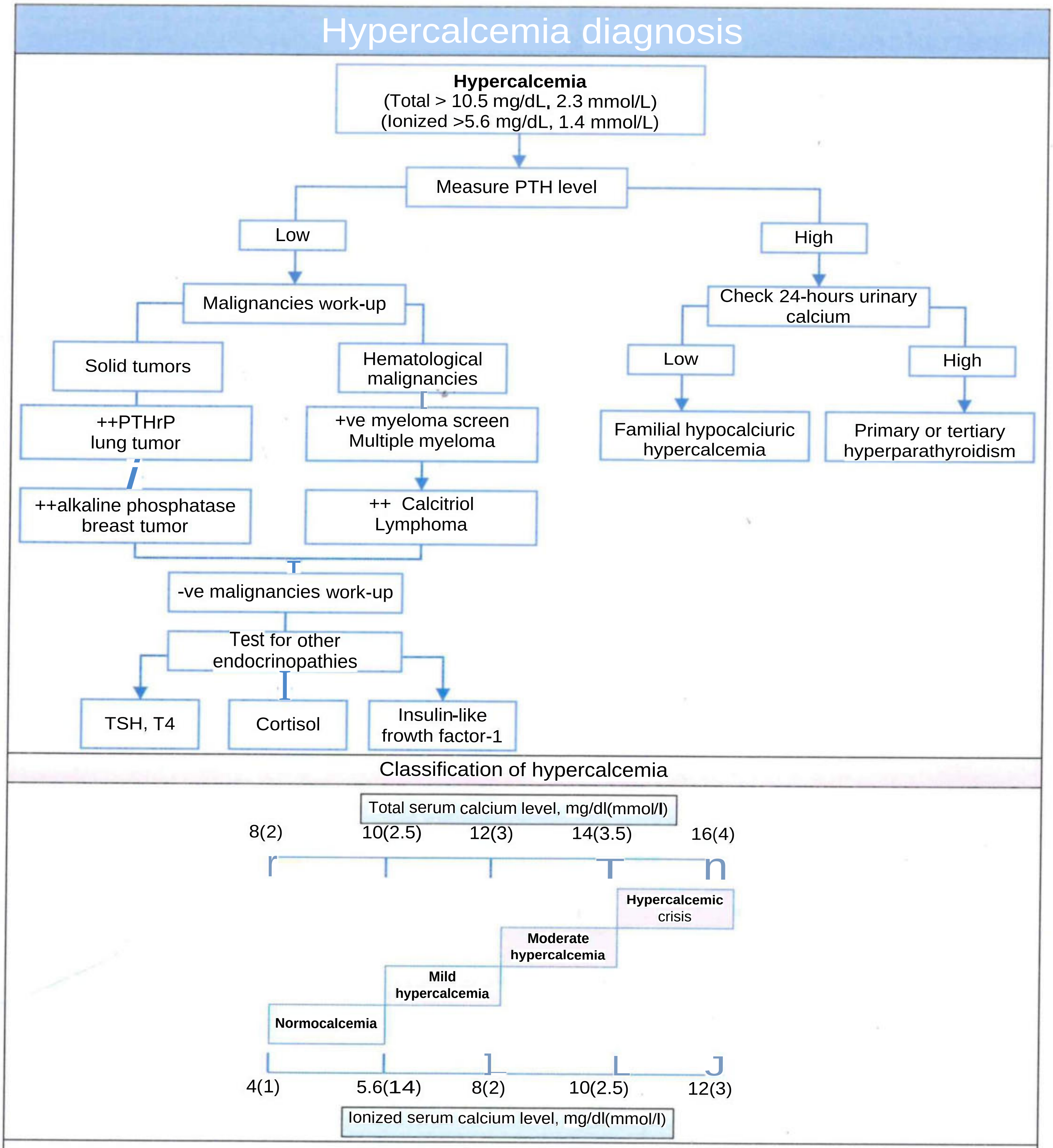
- **Symptoms of hypercalcemia are described in Table 44 -3**

Table 44-3: Manifestation of hypercalcemia

System	Manifestation
Stones (Renal manifestation)	Nephrolithiasis, diabetes insipidus, polyuria,polydipsia
Bones (Skeletal manifestation)	Bone pain, arthritis, osteoporosis
Abdominal moans (GIT manifestation)	Nausea, vomiting, anorexia, constipation, abdominal pain
Prychic groans (Neuromuscular manifestation)	Impaired memory, confusion, muscle weakness
Cardiovascular manifestation	Shortened QT interval, bradycardia, bundle branch block

Diagnosis of hypercalcemia

- **Workup and differential diagnosis of hypercalcemia are described in in Figure 44 -3**


Hypercalcemia diagnosis
Hypercalcemia
(Total > 10.5 mg/dL, 2.3 mmol/L)
(Ionized >5.6 mg/dL, 1.4 mmol/L)
Measure PTH level
Low
High
Malignancies work-up
Check 24-hours urinary calcium
Solid tumors
Hematological malignancies
Low
High
++PTHrP lung tumor
+ve myeloma screen Multiple myeloma
Familial hypocalciuric hypercalcemia
Primary or tertiary hyperparathyroidism
++alkaline phosphatase breast tumor
++ Calcitriol Lymphoma
-ve malignancies work-up
Test for other endocrinopathies
TSH, T4
Cortisol
Insulin-like frowth factor-1
Classification of hypercalcemia
Total serum calcium level, mg/dl(mmol/l)
8(2)
10(2.5)
12(3)
14(3.5)
16(4)
Hypercalcemic crisis
Moderate hypercalcemia
Mild hypercalcemia
Normocalcemia
4(1)
5.6(1.4)
8(2)
10(2.5)
12(3)
Ionized serum calcium level, mg/dl(mmol/l)

Weiss-Guillet EM, Takala J, Jakob SM. Diagnosis and management of electrolyte emergencies. Best Pract Res Clin Endocrinol Metab. 2003;17:623-51
PTH:Parathormone level, PTHrp: Parathyroid hormone releasing proteins

Figure 44-3: diagnosis and severity of hypercalcemia

Treatment of Hypercalcemia

- Isotonic saline, 1–2 l intravenously over a 1-hour period, afterwards approximately 4–6 l/day intravenously
  - » Consider cardiovascular status
- Furosemide, 20– 40 mg intravenously, every 2 hours after correction of dehydration
  - » Anticipate potassium and magnesium depletion, consider water, sodium and chloride loss
  - » Measure urine volume, the urine calcium excretion and serum calcium concentration
  - » Expected fall in S[Ca] concentration: 0.25–0.75 mmol/l [2–6 mg/dl) after 24 hours
- Phosphate
  - » Oral phosphate if serum phosphate < 3 mg/dl
  - » IV phosphate if serum phosphate < 1.5 mg/dl
- Bisphosphonate
  - » Zoledronate [Zometa)
    - 4 mg in 50 ml saline or D5% as a single short infusion over 5–15 minutes intravenously
    - Expected effect after 2 days, median duration of action 33 days
    - Do not repeat dose until after a minimum of 7 days
  - » Pamidronate (Aredia)
    - 60–90 mg in 50–200 ml saline or D5%
    - Expected maximum effect in 2–4 days, median duration of action 2–4 weeks
    - Do not repeat dose until after a minimum of 7 days
- Other lines of therapy
  - » Calcitonin
    - 4–8 IU/kg subcutaneously or intramuscularly every 12 hours
    - Additive effect when given with bisphosphonate
    - Expected lowering in S[Ca] by a maximum of 0.3–0.5 mmol/l [1–2 mg/dl), beginning after 4–6 hours with a nadir within 12–24 hours
    - Effective only in 60–70% of patients, possible tachyphylaxis within 2–3 days
  - » Corticosteroids in vitamin D toxicity, multiple myeloma, lymphoma, granulomatous diseases
    - Hydrocortisone 200–300 mg intravenously for 3–5 days or prednisone 60 mg/day for 10 days
    - Onset of action after 3–5 days
- Consider hemodialysis in S[Ca] concentrations 4.5–5.0 mmol/l [18–20 mg/dl) and neurological symptoms, in patients with heart failure or renal insufficiency

Hyperphosphatemia

- Hyperphosphatemia is considered significant when levels are greater than 1.6 mmol/l [5 mg/dl)

Causes of hyperphosphatemia

- Causes of hyperphosphatemia are described in Table 44 -4

Table 44-4: Causes of hyperphosphatemia

Pseudohyperphosphatemia	Massive acute phosphate load	Renal failure (GFR < 20 – 25 ml/minute)
• Multiple myeloma • Waldenstrom macroglobulinemia • Monoclonal gammopathy • Extreme hypertriglyceridemia • In vitro hemolysis • Hyperbilirubinemia	• Rhabdomyolysis • Tumour-lysis syndrome (Burkitt's • lymphoma, Non-Hodgkin's lymphoma, • leukemias • Hemolysis • Malignant hyperthermia • Ischemic bowel • Lactic acidosis, ketoacidosis • Hyperglycemia • Vitamin D intoxication • Large amounts of phosphate salts	• Hypoparathyroidism • Pseudohypoparathyroidism • Vitamin D intoxication • Acromegaly • Thyrotoxicosis • Glucocorticoid withdrawal or deficiency • Tumoral calcinosis syndrome • Bisphosphonates • Magnesium deficiency

Treatment of hyperphosphatemia

- Saline resuscitation
- Diuretic with acetazolamide
- Remove any drug that cause hyperphosphatemia e.g. Vit D
- Dextrose insulin can be used to make intracellular shift
- In acute hyperphosphatemia, posing a life threatening condition, hemodialysis should be considered, specially if renal function is impaired

References

1. Dépret F, Peacock WF, Liu KD, et al. Management of hyperkalemia in the acutely ill patient. Ann Intensive Care. 2019 Feb 28;9(1):32
2. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. EurD Endocrinol. 2014 25;170:G1-47
3. Guillet E, Takala D, Dakob S Diagnosis and management of electrolyte emergencies. Best Practice & Research Clinical Endocrinology & Metabolism. 2003; 17: 623-651
4. Guise TA, Wysolmerski 3D. Cancer-Associated Hypercalcemia. N Engl D Med. 2022 Apr 14;386(15):1443-1451

Chapter 45

Nutrition protocol

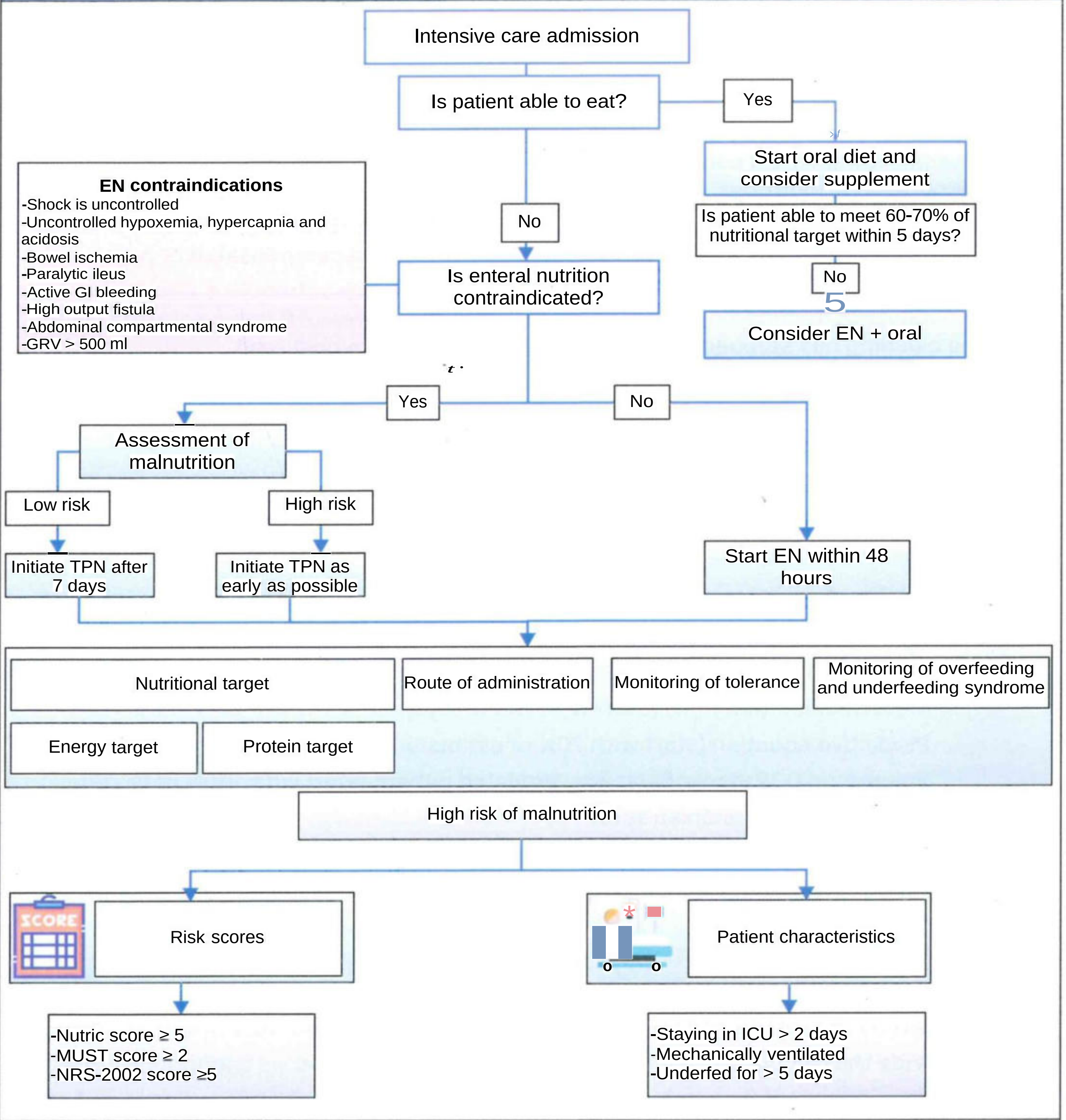
General Principles

- Enteral feeding protocols should be designed and implemented to increase overall percentage of calories provided.

Stepwise approach for starting nutrition in critically ill patient

- All patients should be assessed for caloric and protein requirements upon ICU admission.
    - Energy requirement is 25-30 kcal/kg/d
    - Proteins requirement is 1.2-2.0 g/kg/d
- Consider 20% calories reduction if the patients is sedated or paralyzed
- Patient who is hemodynamically stable and able to eat should start oral feeding within 24 hrs
- If the patient is not able to eat and enteral nutrition (EN) is not contraindicated, EN should be initiated within 48 hours
- If EN is contraindicated we will assess the risk of the patient using risk scores
    - If no risk of malnutrition we can wait for parenteral nutrition (PN) for 7-10 days
    - If at high risk of malnutrition we can start PN as soon as possible
- For both EN and PN, calculation of nutritional targets, monitoring for tolerance and refeeding should be done
- Stepwise approach for nutritional therapy of critically ill patient is illustrated in Figure 45 -1

Nutrition protocol



Intensive care admission

Is patient able to eat?

Yes

Start oral diet and consider supplement

Is patient able to meet 60-70% of nutritional target within 5 days?

No

Consider EN + oral

No

EN contraindications
-Shock is uncontrolled
-Uncontrolled hypoxemia, hypercapnia and acidosis
-Bowel ischemia
-Paralytic ileus
-Active GI bleeding
-High output fistula
-Abdominal compartmental syndrome
-GRV > 500 ml

Is enteral nutrition contraindicated?

Yes

Assessment of malnutrition

Low risk

Initiate TPN after 7 days

High risk

Initiate TPN as early as possible

No

Start EN within 48 hours

Nutritional target

Energy target

Protein target

Route of administration

Monitoring of tolerance

Monitoring of overfeeding and underfeeding syndrome

High risk of malnutrition

Risk scores

-Nutric score ≥ 5
-MUST score ≥ 2
-NRS-2002 score ≥5

Patient characteristics

-Staying in ICU > 2 days
-Mechanically ventilated
-Underfed for > 5 days

Singer P, Blåser AR, Berger MM, et aL ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023:42:1671-1689
EN: enteral nutrition, TPN: total parenteral nutrition, SPN: supplemental parenteral nutrition

Figure 45-1: initiation of nutrition therapy in ICU

Enteral Nutrition

Indications

- All patients should who are not able to eat should start enteral feeding within 24-48 hours of ICU admission

Contraindications

- If shock is uncontrolled and hemodynamic and tissue perfusion goals are not reached, whereas low dose EN can be started as soon as shock is controlled with fluids and vasopressors/inotropes, while remaining vigilant for signs of bowel ischemia.
- In case of uncontrolled life-threatening hypoxemia, hypercapnia or acidosis, whereas EN can be started in patients with stable hypoxemia, and compensated or permissive hypercapnia and acidosis.
- In patients suffering from active upper GI bleeding, whereas EN can be started when the bleeding has stopped and no signs of re-bleeding are observed.
- In patients with overt bowel ischemia.
- In patients with high-output intestinal fistula if reliable feeding access distal to the fistula is not achievable;
- In patients with abdominal compartment syndrome
- If gastric aspirate volume is above 500 ml/6 h.
- Intractable vomiting and diarrhea.

Protocol for initiation and advancement

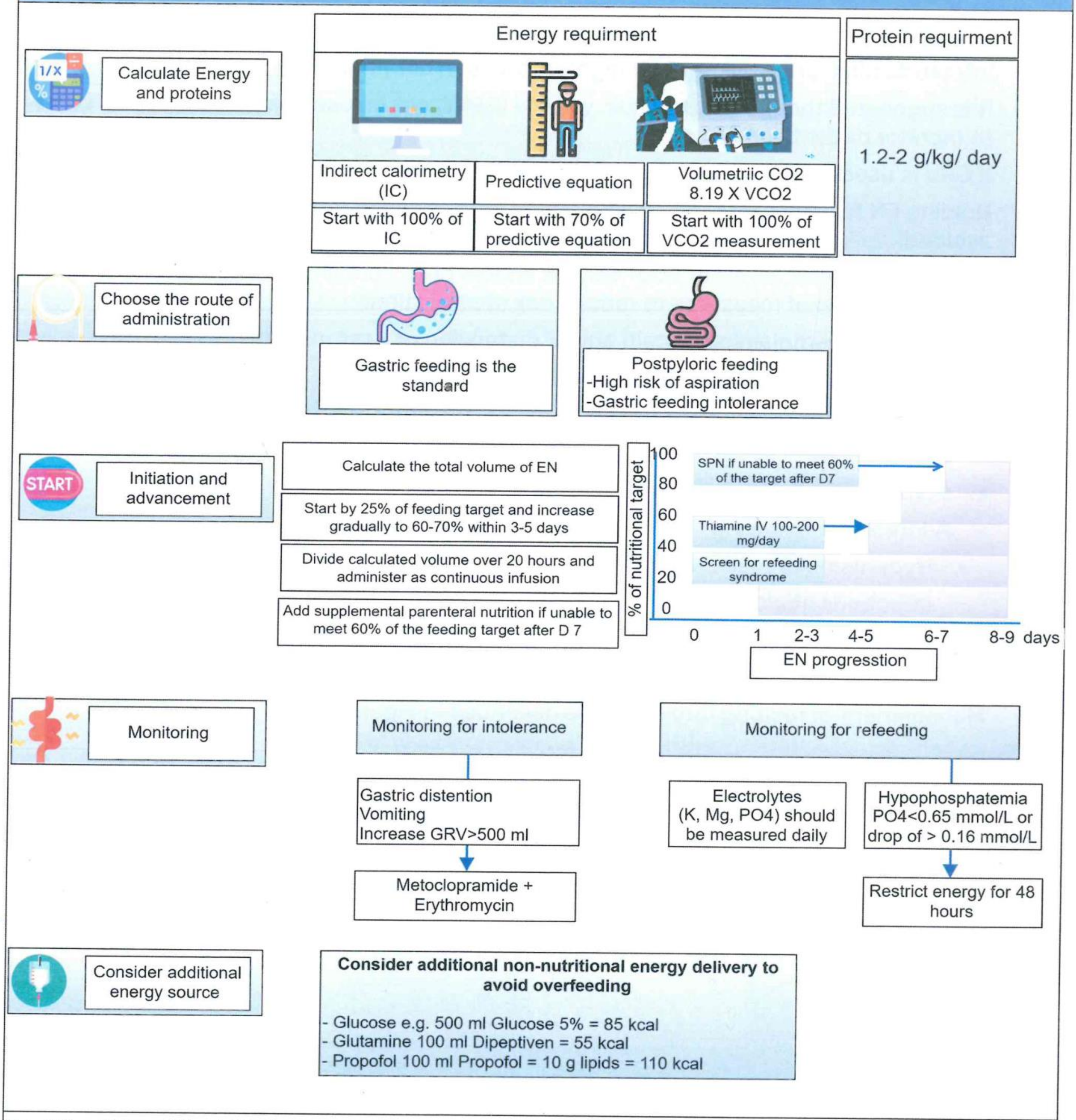
- Calculate the nutritional targets
  - » The required energy can be estimated by
    - Indirect calorimetry (IC) (Start with 100 % of IC)
    - Predictive equation (start with 70% of estimated energy needed)
    - Volumetric C02 in mechanically ventilated patient (start with 100% of VC02)
- Choose the route of administration
  - » Gastric route should be the standard of care
  - » Post-pyloric feeding is indicated in case of high risk of aspiration of intolerance of gastric feeding
- Initiation and advancement
  - » Calculate the total volume of EN
  - » Start by 25% of feeding target and increase gradually to 60-70% within 3-5 days
  - » Divide the calculated volume over 20 hours and administer as continuous infusion
  - » Add supplemental parenteral nutrition if unable to meet 60% of feeding target after 7 days.
- Monitoring of tolerance and refeeding syndrome
- Enteral nutrition protocol is described in Figure 45 -2

Monitor tolerance and refeeding syndrome

Tolerance

- patients should be carefully assessed vomiting, pain, distension, elevated/increasing intraabdominal pressure, and for high gastric residual volume
- It is suggested that gastric residual volume (GRVs) not be used as part of routine care to monitor patients on EN.
- If GRV is used the following recommendations is suggested by ASPEN guidelines
- Holding EN for GRVs >500 mL in absence of other signs of intolerance should be avoided.
- If GRVs monitored, levels of 200- 500mL should raise concern and lead to implementation of measures to reduce risk of aspiration.
- If the patient complaining of pain and or distension or x ray indicate intolerance
- withhold EN until patient is fully resuscitated and/or stable.
- If the Patient having diarrhea defined as > 200 gm stool/day or ≥ 3 liquid stools/day.
  - » Consider use of small peptide formulations in patients with persistent diarrhea
  - » suspected malabsorption, risk for bowel ischemia
  - » Address the following
    - Hyperosmolar medications
    - Infectious etiology, i.e., C. difficile
    - Sensitivity to specific components of the formula
    - Aseptic formula technique
- Management of feeding intolerance is described in Figure 45 -3

Enteral nutrition



Calculate Energy and proteins

Energy requirment

Indirect calorimetry (IC)	Predictive equation	Volumetriic CO2 8.19 X VCO2
Start with 100% of IC	Start with 70% of predictive equation	Start with 100% of VCO2 measurement

Protein requirment

1.2-2 g/kg/ day

Choose the route of administration

Gastric feeding is the standard

Postpyloric feeding
-High risk of aspiration
-Gastric feeding intolerance

Initiation and advancement

Calculate the total volume of EN

Start by 25% of feeding target and increase gradually to 60-70% within 3-5 days

Divide calculated volume over 20 hours and administer as continuous infusion

Add supplemental parenteral nutrition if unable to meet 60% of the feeding target after D 7

SPN if unable to meet 60% of the target after D7

Thiamine IV 100-200 mg/day

Screen for refeeding syndrome

Monitoring

Monitoring for intolerance

Gastric distention
Vomiting
Increase GRV>500 ml

Metoclopramide + Erythromycin

Monitoring for refeeding

Electrolytes (K, Mg, PO4) should be measured daily

Hypophosphatemia PO4<0.65 mmol/L or drop of > 0.16 mmol/L

Restrict energy for 48 hours

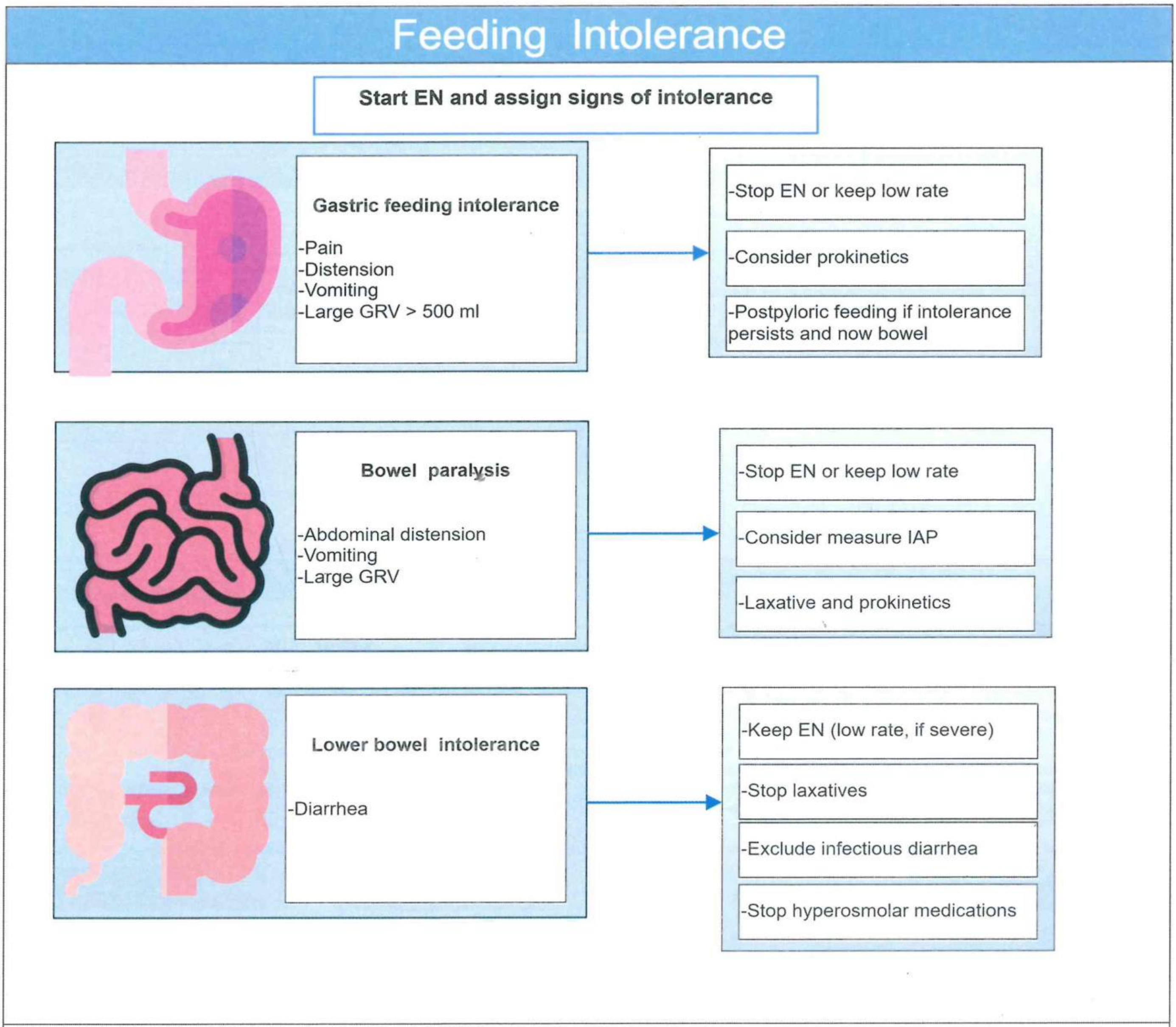
Consider additional energy source

Consider additional non-nutritional energy delivery to avoid overfeeding

- Glucose e.g. 500 ml Glucose 5% = 85 kcal
- Glutamine 100 ml Dipeptiven = 55 kcal
- Propofol 100 ml Propofol = 10 g lipids = 110 kcal

Singer P, Blaser AR, Berger MM, et al.. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023;42:1671-1689

Figure 45-2: Enteral nutrition protocol



Feeding Intolerance

Start EN and assign signs of intolerance

Gastric feeding intolerance

-Pain
-Distension
-Vomiting
-Large GRV > 500 ml

-Stop EN or keep low rate
-Consider prokinetics
-Postpyloric feeding if intolerance persists and now bowel

Bowel paralysis

-Abdominal distension
-Vomiting
-Large GRV

-Stop EN or keep low rate
-Consider measure IAP
-Laxative and prokinetics

Lower bowel intolerance

-Diarrhea

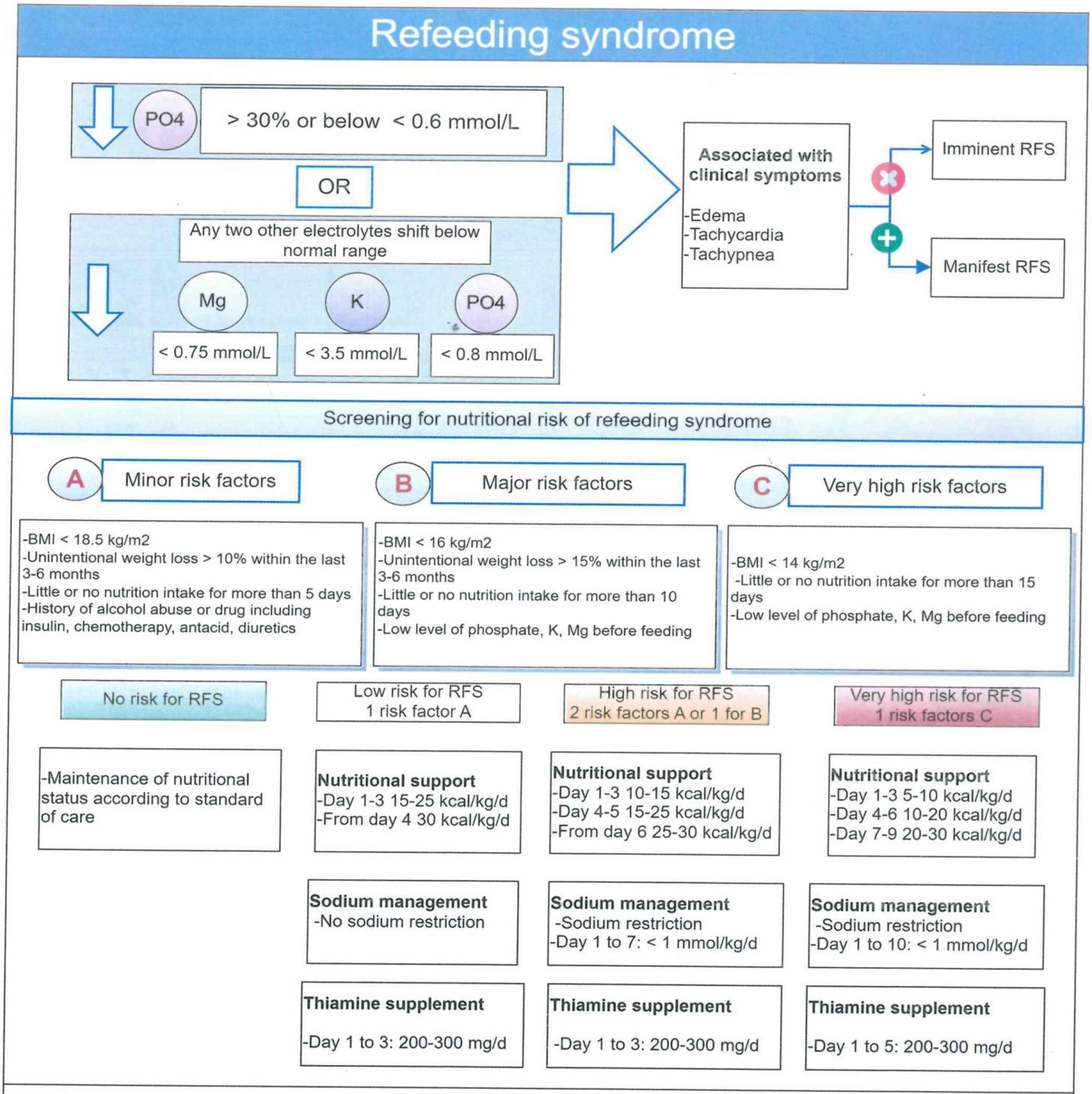
-Keep EN (low rate, if severe)
-Stop laxatives
-Exclude infectious diarrhea
-Stop hyperosmolar medications

Preiser JC, Arabi YM, Berger MM, et al. A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice. Crit Care. 202114;25:424

Figure 45-3: Feeding intolerance management

Refeeding syndrome

- Refeeding syndrome is defined as (serum phosphate (PO4) < 0.65 mmol/l, or a drop from baseline> 0.16 mmol/L occur within 72 hrs of start of enteral nutrition.
- It may result in profound hypophosphatemia, hypokalemia, and hypomagnesemia
- The clinical manifestations of the symptoms of refeeding syndrome are unpredictable and can occur late and without warning.
  - Nausea and vomiting
  - Lethargy
  - Respiratory failure
  - Cardiac failure
  - Hypotension
  - Arrhythmia
  - Delirium and coma
  - Death
- screening and management of refeeding syndrome is illustrated in Figure 45 -4


Refeeding syndrome
PO4
> 30% or below < 0.6 mmol/L
OR
Any two other electrolytes shift below normal range
Mg
K
PO4
< 0.75 mmol/L
< 3.5 mmol/L
< 0.8 mmol/L
Associated with clinical symptoms
-Edema
-Tachycardia
-Tachypnea
Imminent RFS
Manifest RFS
Screening for nutritional risk of refeeding syndrome
A
Minor risk factors
B
Major risk factors
C
Very high risk factors
-BMI < 18.5 kg/m2
-Unintentional weight loss > 10% within the last 3-6 months
-Little or no nutrition intake for more than 5 days
-History of alcohol abuse or drug including insulin, chemotherapy, antacid, diuretics
-BMI < 16 kg/m2
-Unintentional weight loss > 15% within the last 3-6 months
-Little or no nutrition intake for more than 10 days
-Low level of phosphate, K, Mg before feeding
-BMI < 14 kg/m2
-Little or no nutrition intake for more than 15 days
-Low level of phosphate, K, Mg before feeding
No risk for RFS
Low risk for RFS
1 risk factor A
High risk for RFS
2 risk factors A or 1 for B
Very high risk for RFS
1 risk factors C
-Maintenance of nutritional status according to standard of care
Nutritional support
-Day 1-3 15-25 kcal/kg/d
-From day 4 30 kcal/kg/d
Nutritional support
-Day 1-3 10-15 kcal/kg/d
-Day 4-5 15-25 kcal/kg/d
-From day 6 25-30 kcal/kg/d
Nutritional support
-Day 1-3 5-10 kcal/kg/d
-Day 4-6 10-20 kcal/kg/d
-Day 7-9 20-30 kcal/kg/d
Sodium management
-No sodium restriction
Sodium management
-Sodium restriction
-Day 1 to 7: < 1 mmol/kg/d
Sodium management
-Sodium restriction
-Day 1 to 10: < 1 mmol/kg/d
Thiamine supplement
-Day 1 to 3: 200-300 mg/d
Thiamine supplement
-Day 1 to 3: 200-300 mg/d
Thiamine supplement
-Day 1 to 5: 200-300 mg/d

Reber E, Friedli N, Vasiloglou MF, Schuetz P, Stanga Z. Management of Refeeding Syndrome in Medical Inpatients. J Clin Med. 2019 13;8:2202.
PO4: phosphorus, K: potassium, Mg: magnesium, RFS: refeeding syndrome

Figure 45-4: Management of nutritional therapy according to risk of refeeding syndrome

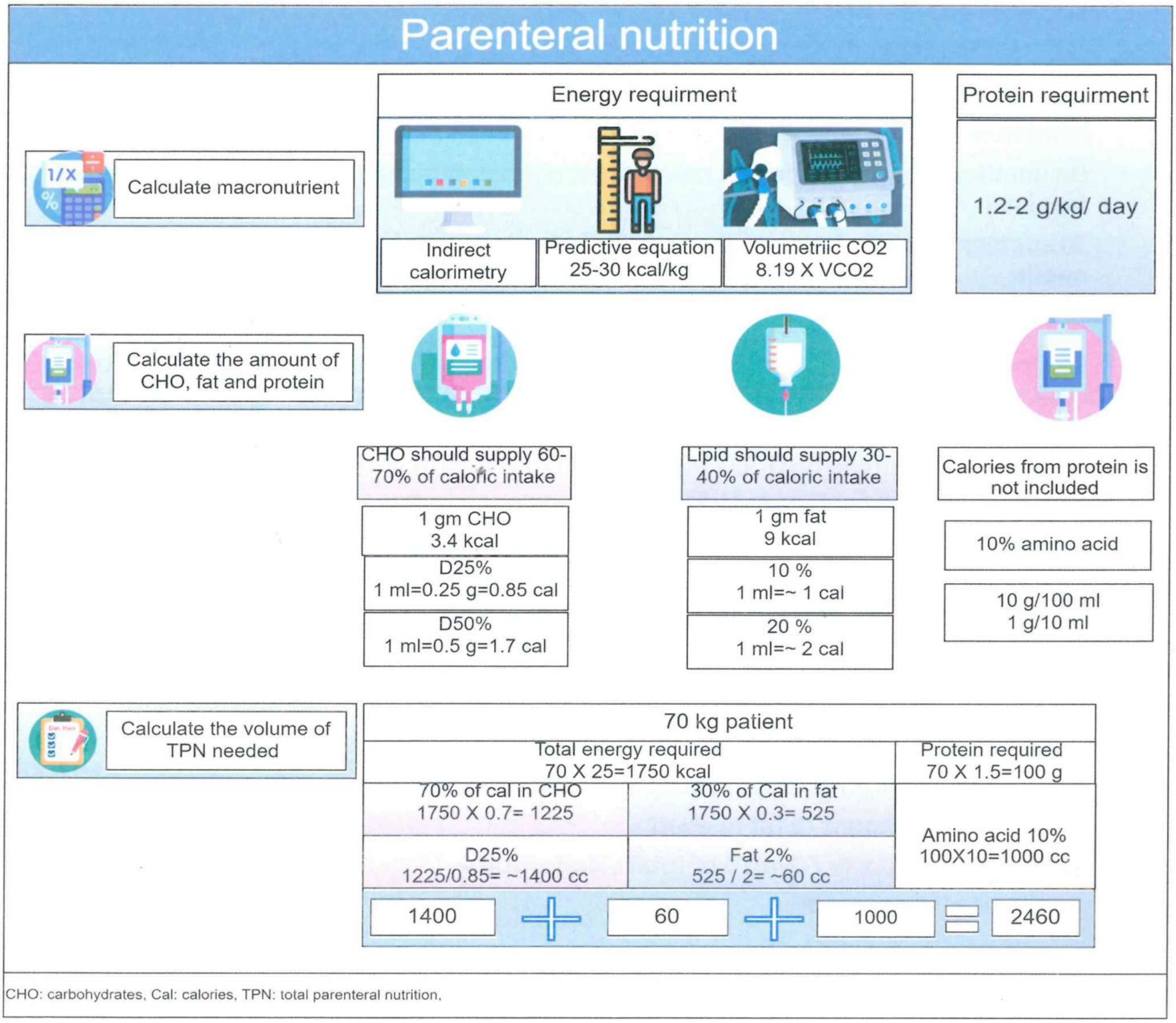
Parenteral Nutrition

Indication

- In the low nutritional risk patient, PN should be withheld for 7 days following ICU admission for the patient who cannot maintain volitional intake or receive EN.
- On admission in high nutrition risk or severely malnourished patients, when EN is not feasible.
- To supplement EN after 7-10 days of EN if unable to meet > 60% of energy and protein needs.

Initiation and advancement

- PN dosing (≤20 kcal/kg/d or 80% of estimated energy needs] with adequate protein (≥1.2 g protein/kg/d] be considered in appropriate patients requiring PN, initially over the first week of hospitalization in the ICU.
- Parenteral glutamine SHOULD NOT be used routinely in critical care setting.
- Calculate the total energy needed (Non-protein energy)
- Start by 20 kcal/kg/day
- Calculate the amount of CHO needed
  - » Carbohydrate (CHO) should supply 60-70% of total caloric intake
  - » CHO is given as dextrose monohydrate, which yields 3.4 Kcal/gram
  - » MAXIMUM rate of CHO administration should not exceed 5 mg CHO/Kg/min.
  - » For 70-kg patient maximum amount of CHO we can use is 500 gm/day
  - » Carbohydrate (CHO) should supply 60-70% of total caloric intake
- Calculate the amount of fat needed
  - » Fat should supply 30-40% of total caloric intake
  - » Fat has 9 Kcal/gram
  - » Normal fat requirement is 1-2.5 gm/d
  - » MAXIMAL tolerance level of lipid is considered to be 2.5 gm/Kg body weight and 60% of energy from fat is also considered to be upper limit
- Estimate protein needs is to use the non-protein energy
  - » Start by 1.2 g/kg/d
- Estimate the amount of fluid needed
- ~30 ml/kg/d
  - » Total parenteral nutrition calculation is illustrated in Figure 45 -5



Parenteral nutrition

Calculate macronutrient

Energy requirment			Protein requirment
Indirect calorimetry	Predictive equation 25-30 kcal/kg	Volumetriic CO2 8.19 X VCO2	1.2-2 g/kg/ day

Calculate the amount of CHO, fat and protein

CHO should supply 60-70% of caloric intake	Lipid should supply 30-40% of caloric intake	Calories from protein is not included
1 gm CHO 3.4 kcal	1 gm fat 9 kcal	10% amino acid
D25% 1 ml=0.25 g=0.85 cal	10 % 1 ml=~ 1 cal	10 g/100 ml 1 g/10 ml
D50% 1 ml=0.5 g=1.7 cal	20 % 1 ml=~ 2 cal	

Calculate the volume of TPN needed

70 kg patient		
Total energy required 70 X 25=1750 kcal		Protein required 70 X 1.5=100 g
70% of cal in CHO 1750 X 0.7= 1225	30% of Cal in fat 1750 X 0.3= 525	Amino acid 10% 100X10=1000 cc
D25% 1225/0.85= ~1400 cc	Fat 2% 525 / 2= ~60 cc	

1400 + 60 + 1000 = 2460

CHO: carbohydrates, Cal: calories, TPN: total parenteral nutrition,

Figure 45-5:TPN calculation

Administration

- High osmolarity PN through central line
- Low osmolarity (< 850 mOsmol/L) PN can be administrated through dedicated peripheral venous line

Monitoring

- Schedule for laboratory is described in Table 45 -1

Table 45-1: Lab monitoring in PN

	Baseline	First week			Stable PN
		Daily	Twice weekly	Weekly	Weekly
Glucose	√	√			√
Na	√	√			√
K	√	√			√
Ca	√	√			√
Mg	√	√			√
P04	√	√			√
Urea and creatinine	√	√			√
ALT, AST	√				√
Alkaline ph	√		√		√
GGT	√				
Bilirubin	√		√		√
Albumin	√		√		√
CBC	√			√	
Triglycerides				√	
Copper, zinc, ferritin					After 1 month then every 3 months
Thyroid function					Every 6 months

Vascular access and administration

- Types of vascular access that are used for PN administration are described in Table 45 -2

Table 45-2: Vascular access used in PN administration

Type of VAD	Placement	Limitations	Advantages
Short peripheral catheter	Percutaneous peripheral insertion.	Infusion < 600 mOsm/L, high risk of phlebitis.	Easy to place, cost, lower infection risk.
Midline	Percutaneous peripheral insertion.	Not appropriate for infusions > 900 mOsm/L	Lasting 2-4 weeks
PICC	Percutaneous peripheral insertion.	Self-care difficult, uncomfortable for long periods	Used in acute and home care settings. Lasting for 3 months
Nontunneled central VAD	Subclavian, jugular or femoral vein.	Operating room or hospital setting for placement.	Easy self-care
Tunneled central VAD	Subclavian, jugular or (Heckman)	Hospital setting, small procedure for removal.	Lower risk of infection

Nutrition therapy in special population

Obese patients

- Energy requirement:
  - 11-14 kcal/kg/d of actual body weight for BMI 30-50
  - 22-25 kcal/kg/d of ideal body weight for BMI > 50
- Protein requirement
  - 2.0 g/kg/d of ideal body weight for BMI 30-40
  - 2.5 g/kg/d of ideal body weight for BMI > 40

Non-intubated patient not reaching the energy target

- oral nutritional supplements should be considered first and then enteral
- In non-intubated patients with dysphagia and swallowing is proven unsafe, enteral should be administered

Burns

- Glucose is provided at 5-7 mg/kg/min which represents 50% of total caloric intake
- Protein are provided at 1.5-2 g/day
- Consider enteral glutamine (0.3-0.5 g/kg/d) in patients with burns > 20% body surface area for 10-15 days

Liver failure

- Standard enteral formulations be used in ICU patients with acute and chronic liver disease
- no evidence of further benefit of branched-chain amino acid (BCAA) formulations on coma grade in the ICU

Respiratory failure

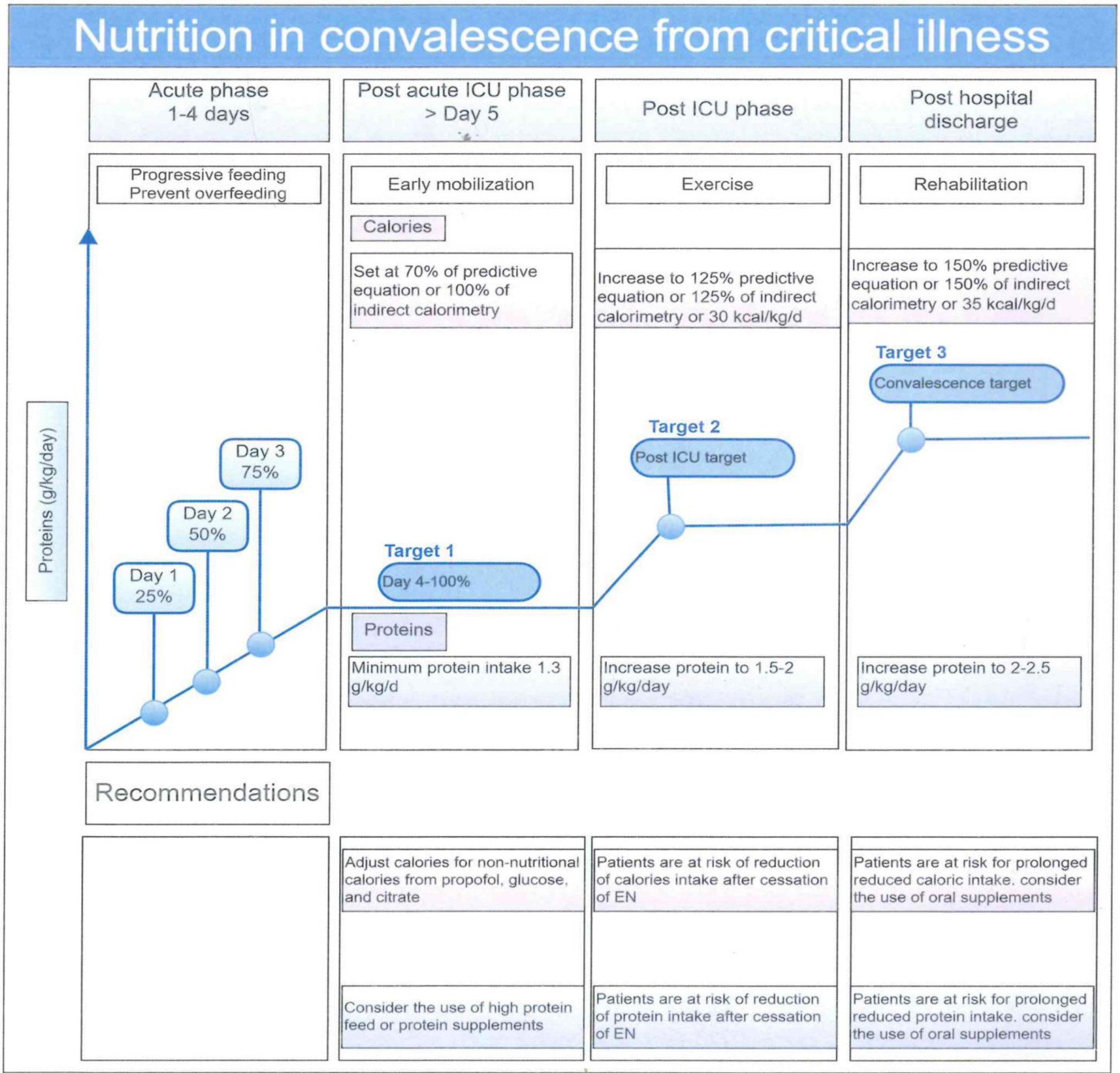
- Specially high-lipid low-carbohydrate formulations designed to manipulate the respiratory quotient and reduce C02 production **ARE NOT RECOMMENDED** for routine use in ICU patients with acute respiratoryfailure.
- No recommendation regarding the use of anti inflammatory lipid profile (i.e., omega-3 fish oils, borage oil) and antioxidants in patient with ARDS.

Acute Kidney Injury (AKI)

- Patient presented with AKI should be placed on a standard enteral formulation and that standard ICU recommendations for protein (1.2–2 g/kg actual body weight per day) and energy (25–30 kcal/kg/d).
- Patients who are receiving frequent hemodialysis or continuous renal replacement therapy should receive increased protein, up to a maximum of 2.5 g/kg/day
- Protein should not be restricted in patients with renal insufficiency as a mean to avoid or delay initiation of dialysis therapy.

Nutrition during phases of critical illness and convalescence therapy

- In the early phase, gradual progression of calories and proteins to target is recommended while monitoring phosphate for refeeding hypophosphatemia
- During the further patient journey, more calories and proteins should be prescribed
- Even after ICU and hospital discharge, increased levels of calories and proteins are necessary to recover, probably for prolonged periods.
- Recommendations for calories and proteins during different phases of critical illness and convalescence are presented in Figure 45-6


Nutrition in convalescence from critical illness
Acute phase 1-4 days
Post acute ICU phase > Day 5
Post ICU phase
Post hospital discharge
Progressive feeding
Prevent overfeeding
Early mobilization
Exercise
Rehabilitation
Calories
Proteins (g/kg/day)
Day 1 25%
Day 2 50%
Day 3 75%
Target 1
Day 4-100%
Target 2
Post ICU target
Target 3
Convalescence target
Proteins
Recommendations

Set at 70% of predictive equation or 100% of indirect calorimetry

Increase to 125% predictive equation or 125% of indirect calorimetry or 30 kcal/kg/d

Increase to 150% predictive equation or 150% of indirect calorimetry or 35 kcal/kg/d

Minimum protein intake 1.3 g/kg/d

Increase protein to 1.5-2 g/kg/day

Increase protein to 2-2.5 g/kg/day

Adjust calories for non-nutritional calories from propofol, glucose, and citrate

Patients are at risk of reduction of calories intake after cessation of EN

Patients are at risk for prolonged reduced caloric intake. consider the use of oral supplements

Consider the use of high protein feed or protein supplements

Patients are at risk of reduction of protein intake after cessation of EN

Patients are at risk for prolonged reduced protein intake. consider the use of oral supplements

Van Zanten ARH, De Waele E, Wischmeyer PE. Nutrition therapy and critical illness: Practical guidance for the ICU, post-ICU, and long-term convalescence phases. Crit Care. 2019;23:368.
EN: Enteral nutrition

Figure 45-6: Approach to Provide Proteins and Calories During the Phases of Critical Illness and convalescence (adapted from van Zanten ARH, et al 3)

References

1. Compher C, Bingham AL, McCall M. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. OPEN D Parenter Enteral Nutr. 2022:46:12-41
2. Preiser DC, Arabi YM, Berger MM, A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice. Crit Care. 2021:25:424
3. van Zanten ARH, De Waele E, Wischmeyer PE. Nutrition therapy and critical illness: practical guidance for the ICU, post-ICU, and long-term convalescence phases. Crit Care. 2019:23:368.
4. Singer P, Blåser AR, Berger MM, et al.. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023:42:1671-1689
5. Taylor BE, McClave SA, Martindale RG et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Crit Care Med. 2016 44:390-438
6. Singer P, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019: 38:48-79.

SECTION 11

Cardiovascular pathophysiology in critically ill patients

Chapter 46

Tachyarrhythmia & Bradyarrhythmia

Tachy-Arrhythmia

Definition

- Tachyarrhythmia is defined as heart rate above 100 /min
- Narrow complex tachycardia is defined QRS duration <0.12 sec
- Wide complex tachycardia is defined as QRS duration ≥ 0.12 sec
- Unstable tachycardia if the patient developed one or more of the following symptoms
  - Hypotension
  - Syncope
  - Light-headedness
  - Heart failure
  - Shock
  - Myocardial infarction
  - Pulmonary edema

Supraventricular tachycardia types and pathophysiology

Atrial tachyarrhythmias include the following:

- Sinus tachycardia
- Inappropriate sinus tachycardia (IST)
- Atrial tachycardia
- Multifocal atrial tachycardia
- Atrial flutter
- Atrial fibrillation

AV tachyarrhythmias include the following:

- AV nodal reentrant tachycardia (AVNRT)
- AV reentrant tachycardia (AVRT)
- Types and mechanisms of SVT are described in Figure 46 -1

Supraventricular tachycardia diagnosis

- Diagnosis of SVT is described in Figure 46 -2

Diagnosis of wide complex tachycardia

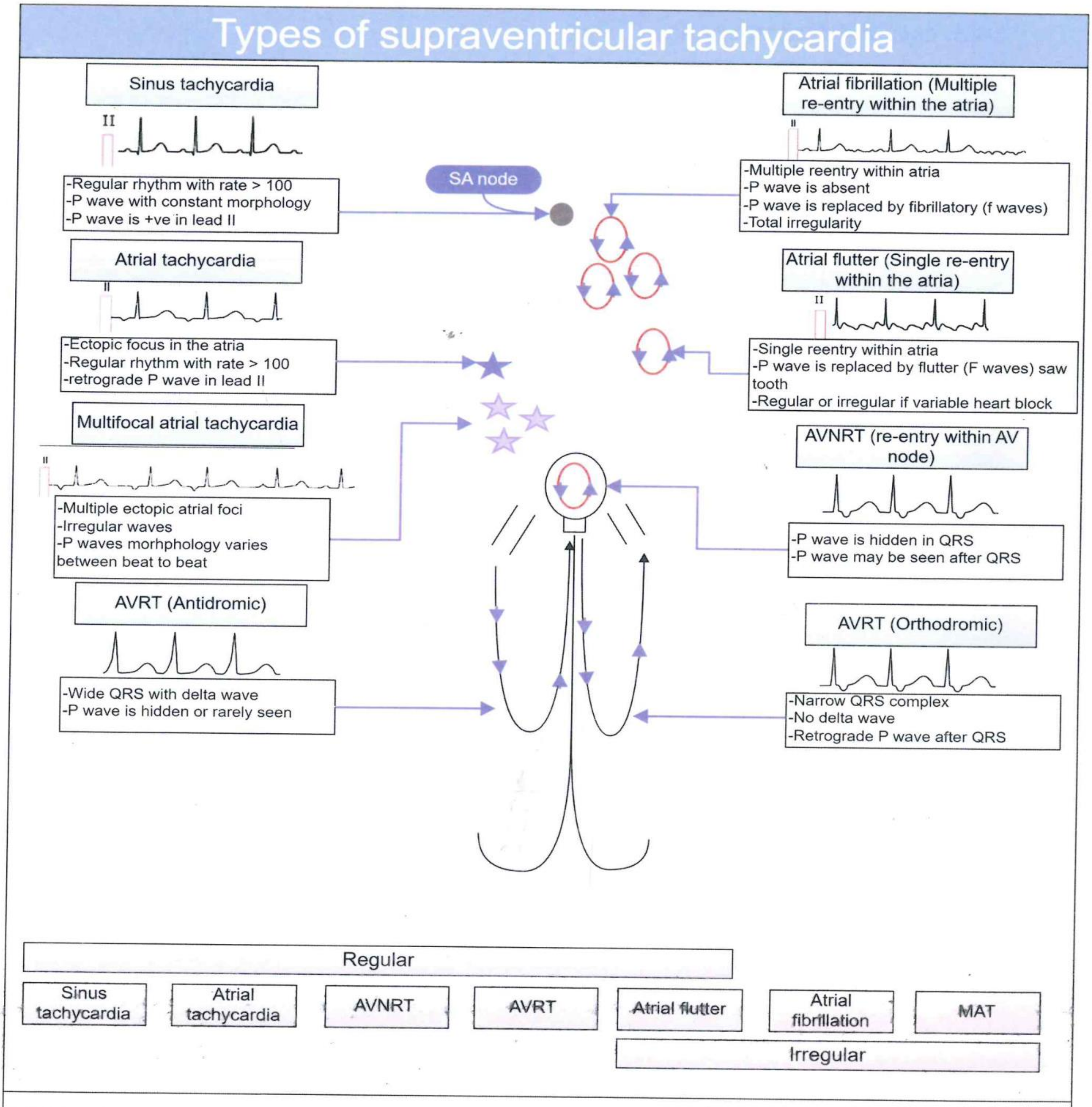
Criteria for Diagnosis

- Concordance: Is there concordance (monophasic with same polarity) in all of the precordial leads? If yes, then VT.

- AV Dissociation: Is there evidence of AV dissociation (fusion or capture beats)? If yes, then VT.
- Bundle-branch morphology: Is the QRS morphology in V1 and V6 consistent with either LBBB or RBBB? If no, then VT
- Differentiation between SVT and ventricular tachycardia is described in Figure 46 -3

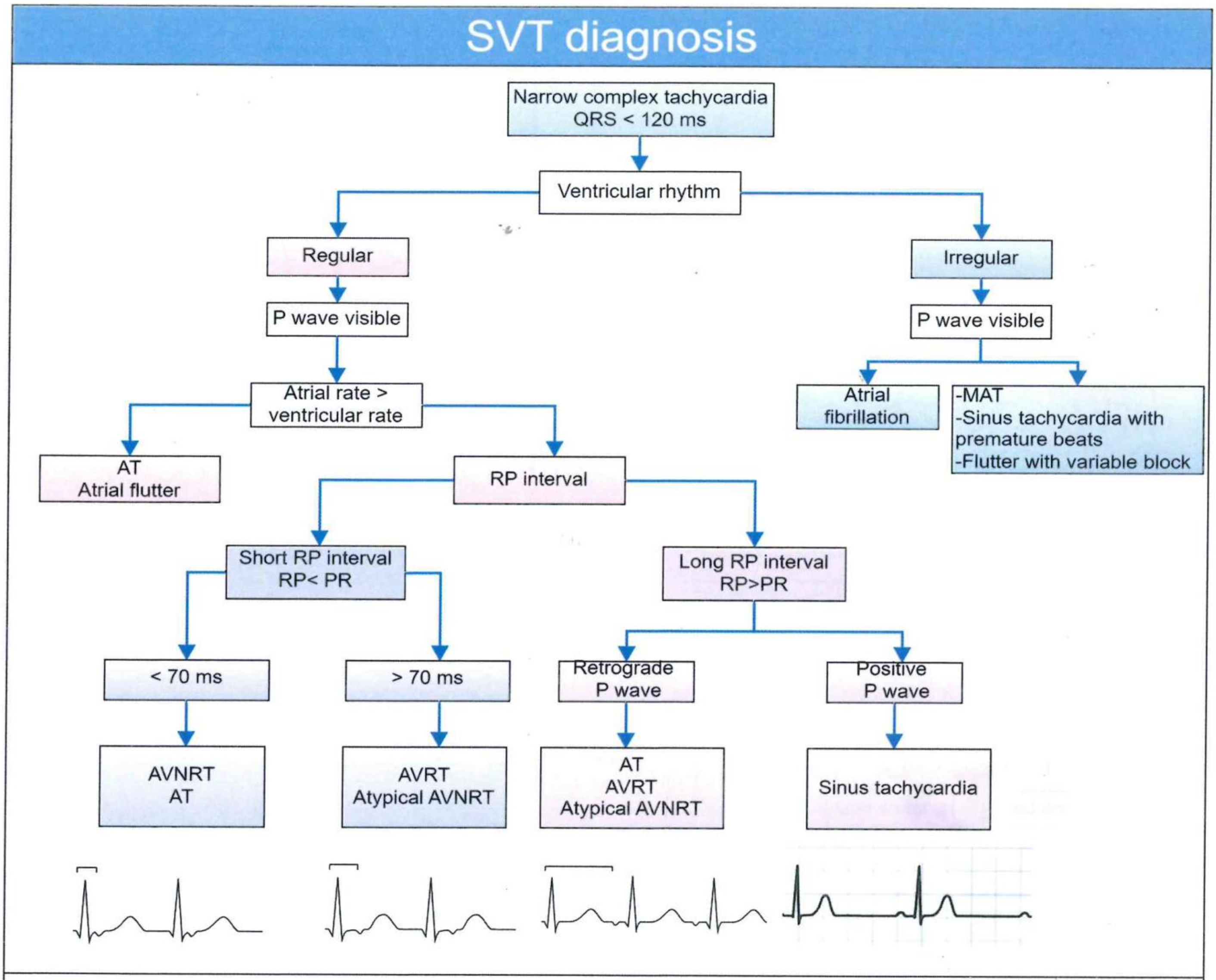
Management of tachyarrhythmia

- SVT management is described in Figure 46 -4 and Table 46 -1


Types of supraventricular tachycardia
Sinus tachycardia
II
-Regular rhythm with rate > 100
-P wave with constant morphology
-P wave is +ve in lead II
SA node
Atrial tachycardia
II
-Ectopic focus in the atria
-Regular rhythm with rate > 100
-retrograde P wave in lead II
Multifocal atrial tachycardia
II
-Multiple ectopic atrial foci
-Irregular waves
-P waves morhphology varies between beat to beat
AVRT (Antidromic)
-Wide QRS with delta wave
-P wave is hidden or rarely seen
Atrial fibrillation (Multiple re-entry within the atria)
II
-Multiple reentry within atria
-P wave is absent
-P wave is replaced by fibrillatory (f waves)
-Total irregularity
Atrial flutter (Single re-entry within the atria)
II
-Single reentry within atria
-P wave is replaced by flutter (F waves) saw tooth
-Regular or irregular if variable heart block
AVNRT (re-entry within AV node)
-P wave is hidden in QRS
-P wave may be seen after QRS
AVRT (Orthodromic)
-Narrow QRS complex
-No delta wave
-Retrograde P wave after QRS
Regular
Sinus tachycardia
Atrial tachycardia
AVNRT
AVRT
Atrial flutter
Atrial fibrillation
MAT
Irregular

AVRT: Atrioventricular renentrant tachycardia, AVNRT: Atrioventricula nodal renentrant tachycardia, MAT multifocal atrial tahycardia

Figure 46-1:Tachyarrhythmia types and pathophysiology


SVT diagnosis
Narrow complex tachycardia
QRS < 120 ms
Ventricular rhythm
Regular
Irregular
P wave visible
P wave visible
Atrial rate > ventricular rate
Atrial fibrillation
-MAT
-Sinus tachycardia with premature beats
-Flutter with variable block
AT
Atrial flutter
RP interval
Short RP interval
RP< PR
Long RP interval
RP>PR
< 70 ms
> 70 ms
Retrograde P wave
Positive P wave
AVNRT
AT
AVRT
Atypical AVNRT
AT
AVRT
Atypical AVNRT
Sinus tachycardia

Shah RL, Badhwar N. Approach to narrow complex tachycardia: non-invasive guide to interpretation and management. Heart. 2020;106:772-783
AT: atrial tachycardia, AVRT: Atrioventricular renentrant tachycardia, AVNRT: Atrioventricula nodal renentrant tachycardia, MAT: multifocal atrial tachycardia

Figure 46-2:Diagnosis of SVT

Diagnosis of wide complex tachycardia

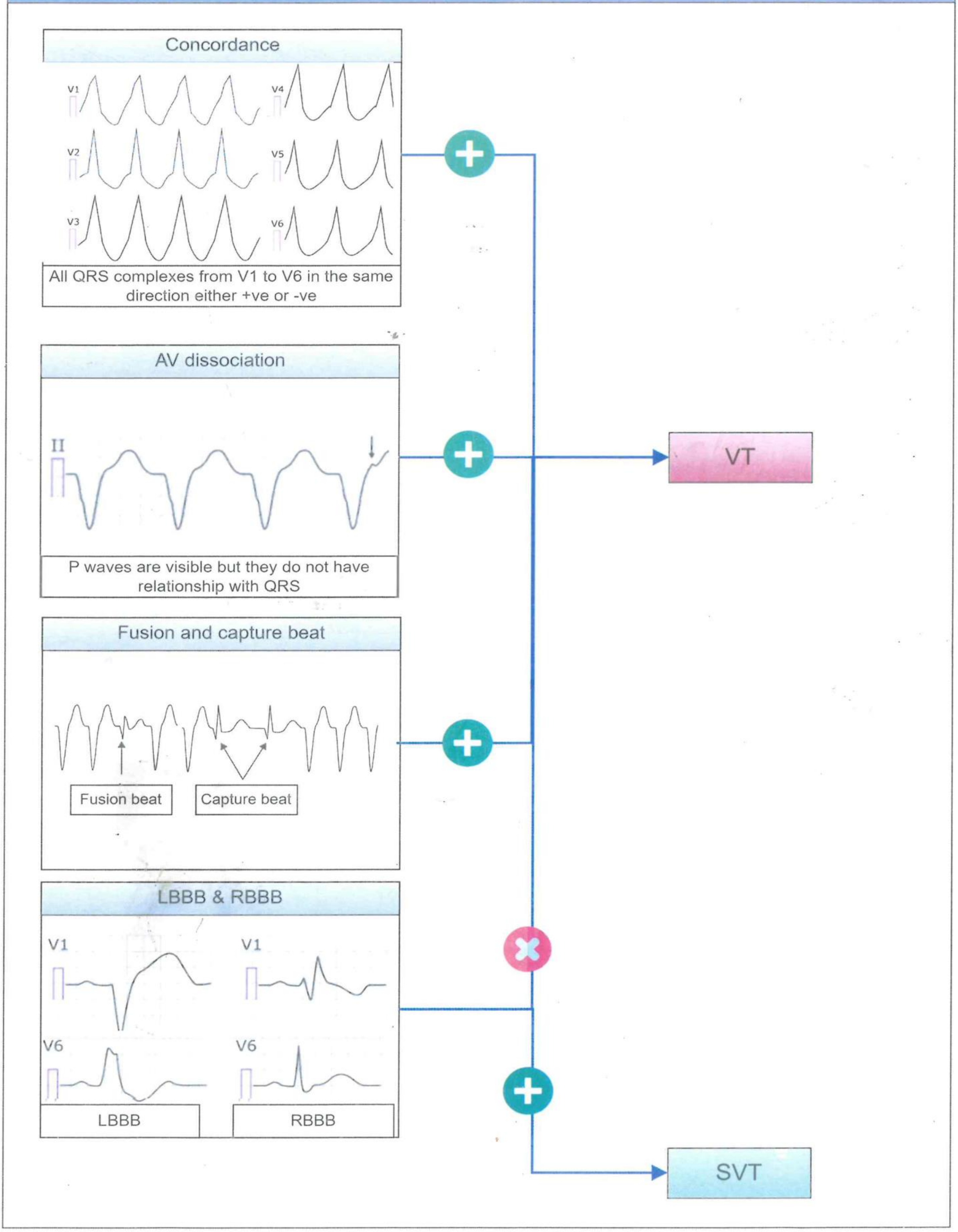
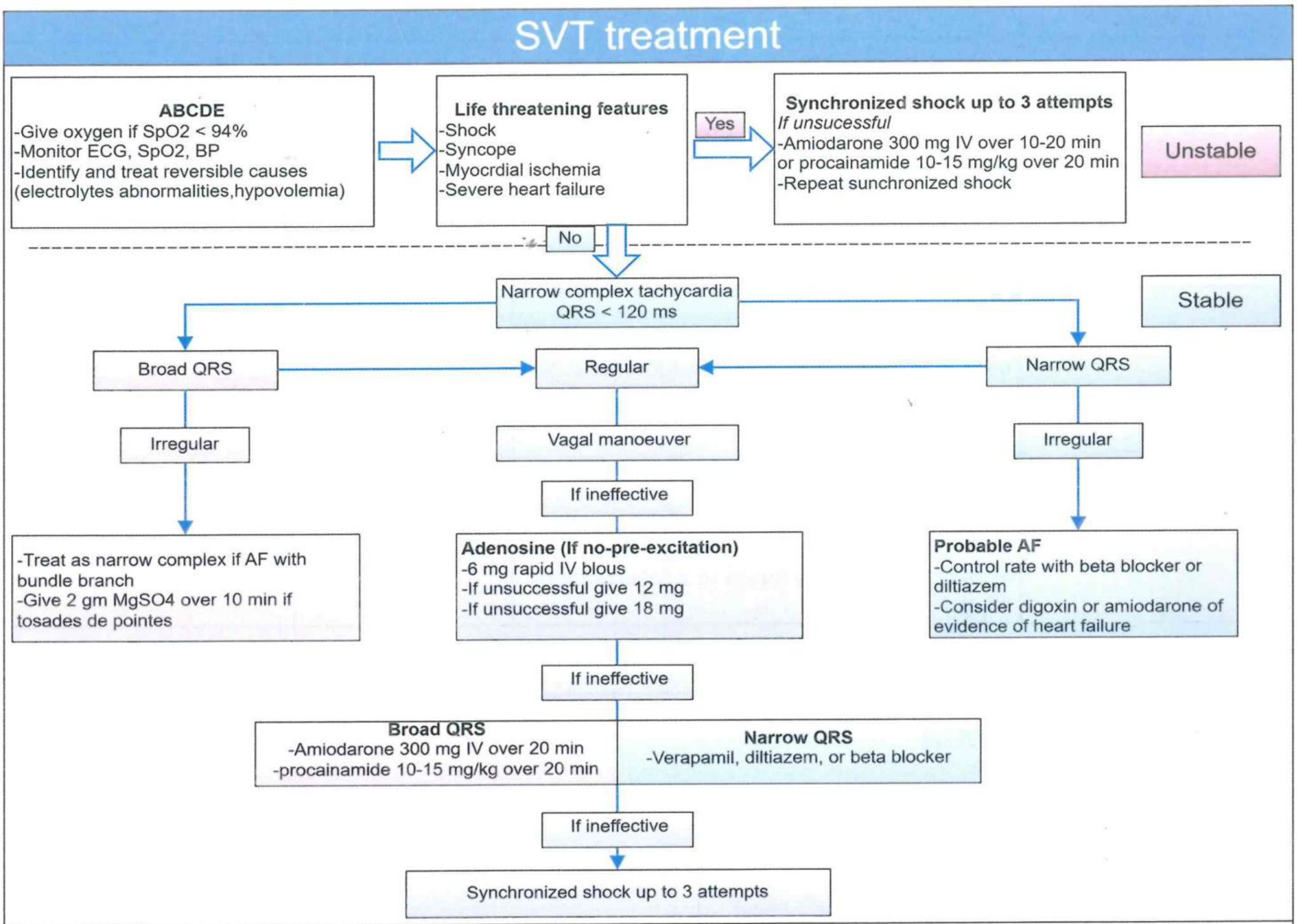

Concordance
V1
V2
V3
V4
V5
V6
All QRS complexes from V1 to V6 in the same direction either +ve or -ve
AV dissociation
II
P waves are visible but they do not have relationship with QRS
Fusion and capture beat
Fusion beat
Capture beat
LBBB & RBBB
V1
V1
V6
V6
LBBB
RBBB
VT
SVT

Figure 46-3: diagnosis of wide complex tachycardia


SVT treatment
ABCDE
-Give oxygen if SpO2 < 94%
-Monitor ECG, SpO2, BP
-Identify and treat reversible causes
(electrolytes abnormalities,hypovolemia)
Life threatening features
-Shock
-Syncope
-Myocrdial ischemia
-Severe heart failure
Yes
Synchronized shock up to 3 attempts
If unsucessful
-Amiodarone 300 mg IV over 10-20 min
or procainamide 10-15 mg/kg over 20 min
-Repeat sunchronized shock
Unstable
No
Narrow complex tachycardia
QRS < 120 ms
Stable
Broad QRS
Regular
Narrow QRS
Irregular
Vagal manoeuver
Irregular
If ineffective
-Treat as narrow complex if AF with bundle branch
-Give 2 gm MgSO4 over 10 min if tosades de pointes
Adenosine (If no-pre-excitation)
-6 mg rapid IV blous
-If unsuccessful give 12 mg
-If unsuccessful give 18 mg
Probable AF
-Control rate with beta blocker or diltiazem
-Consider digoxin or amiodarone of evidence of heart failure
If ineffective
Broad QRS
-Amiodarone 300 mg IV over 20 min
-procainamide 10-15 mg/kg over 20 min
Narrow QRS
-Verapamil, diltiazem, or beta blocker
If ineffective
Synchronized shock up to 3 attempts

Soar J, Böttiger BW, Carli P, et al. European Resuscitation Council Guidelines 2021: Adult advanced life support. Resuscitation. 2021;161:115-151
AF: atrial fibrillation

Figure 46-4: Tachyarrhythmia management

Table 46-1: Management of SVT

	Narrow complex tachycardia		Wide complex tachycardia	
Hemodynamic unstable	Synchronized cardioversion		Synchronized cardioversion	Defibrillation
	Narrow regular	Narrow irregular	Wide regular	Wide irregular
	50-100	120-200 D biphasic or 200 0 monophasic	100 J	Defibrillation (NOT synchronized)
Hemodynamic stable	Vagal manoeuvres, preferably in the supine position with leg elevation			
	Adenosine (6-18 mg i.v. bolus) is recommended if vagal manoeuvres fail.			
	Verapamil : 5-10 mg bolus over 2 min if no response -> additional 10 mg 15-30 min after initial dose		Procainamide 20-50 mg/min until arrhythmia suppressed, hypotension ensue, QRS duration > 70 ms, or maximum dose > 17 mg/kg given Maintenance infusion: 1-4 mg/min Avoid if prolonged QT or congestive heart failure	
	Diltiazem: 0.25 mg/kg (15-20 mg) IV bolus over 2 mi. if no response -> additional 0.35 mg/kg (20-25 mg) 15-30 min after initial dose		Amiodarone: 150 mg every 10 min. repeat as needed if VT recurs to maximum dose of 2.2 g in 24 hours Maintenance infusion: 1 mg/min for the first 6 hrs considered if vagal manoeuvres and adenosine fail	
	Beta-blockers Metoprolol: 2.5-5 mg bolus over 2 min if no response -> additional 5 mg may be administered every 5 min to a total dose of 15 mg		Sotalol: 100 mg (1.5 mg/kg) over 5 min. avoid if prolonged QT	
	Synchronized direct-current cardioversion is recommended when drug therapy fails to convert or control the tachycardia			

Brady-Arrhythmia

Definition:

- heart rate < 60 beats/min

Types:

- Sinus rhythm: upright P-wave in I, II, aV; inverted P-wave in aVR
- Sinoatrial node dysfunction (sick sinus syndrome, SSS)
  - Sinus bradycardia
  - Sinus arrest
  - Tachy-brady syndrome (sinus bradycardia/arrest interspersed with SVT)

Atrioventricular block

- 1st degree: PR prolongation, rarely symptomatic
- 2nd degree: Intermittent interruption of conduction of atrial impulses to ventricles
  - Type 1: progressive PR prolongation leading to interrupted conduction
  - Type 2: fixed PR interval with interrupted conduction
- 3rd degree: atrioventricular dissociation

Slow AF

- Irregular RR interval without recognizable P-wave

Important Historical Features

- Fever/travel
- Chest pain
- Cold intolerance, weight gain
- Headache, AMS, trauma
- Abdominal pain/distension
- Medication changes

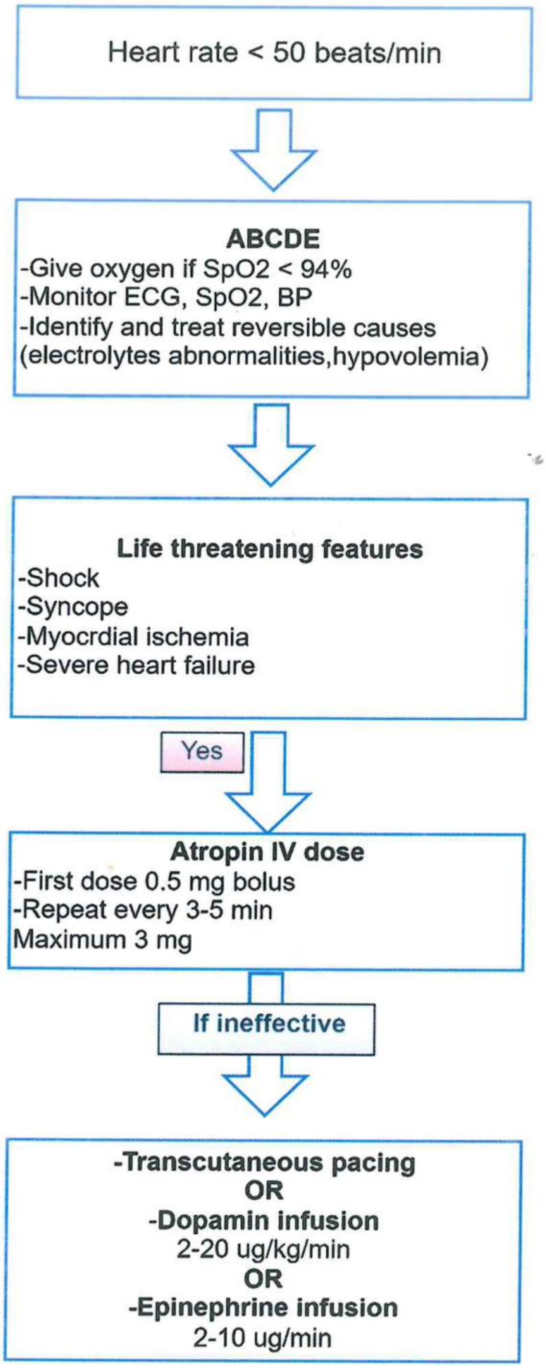
Important Examination Findings

- Perfusion (temperature, capillary refill)
- Presence of fistula or hemodialysis catheter
- Existing device (malfunction)

Management

- If unstable:
    - » ABC
    - » Oxygen therapy
    - » Atropine 0.5mg IV q3-5min (maximum 3mg)
    - » Dopamine 5-20 pg/kg/min
    - » Epinephrine infusion 2-10 pg/min
- Management of bradyarrhythmia is described in Figure 46-5

Bradyarrhythmia management



Heart rate < 50 beats/min

ABCDE
-Give oxygen if SpO2 < 94%
-Monitor ECG, SpO2, BP
-Identify and treat reversible causes
(electrolytes abnormalities,hypovolemia)

Life threatening features
-Shock
-Syncope
-Myocrdial ischemia
-Severe heart failure

Yes

Atropin IV dose
-First dose 0.5 mg bolus
-Repeat every 3-5 min
Maximum 3 mg

If ineffective

-Transcutaneous pacing
OR
-Dopamin infusion
2-20 ug/kg/min
OR
-Epinephrine infusion
2-10 ug/min

Causes Hs and Ts	Management
Hypovolemia	Infusion of normal saline
Hypoxia	Airway management and oxygenation
Hydrogen ion excess (acidosis)	Hyperventilation & NaHCO3
Hypoglycemia	IV use of dextrose
Hyperkalemia	IV CaCl IV NaHCO3
Hypothermia	Gradual warming
Hyperkalemia	IV CaCl IV NaHCO3
Tension pneumothoax	Needle thoracostomy
Tamponade	Pericardiocentesis
Toxins/drugs	Based on specific agent
Thrombosis (Pulmonary)	Fibrinolysis/ embolectomy
Thrombosis (Cardiac)	Depend on extent and age of MI

Toxins/drugs
Beta blocker -Glucagon 5 mg IV -Insulin 1 U/kg + Dextrose -intralipid 1.5 ml/kg
Calcium channel blocker -Glucagon 5 mg IV -Insulin 1 U/kg + Dextrose -intralipid 1.5 ml/kg
Digoxin -Digoxin immune tab

Neumar RW, Otto CW, Link MS, et al. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122(18 Suppl 3):S729-67

Figure 46-5: Bradyarrhytmia management

Chapter 47

Atrial fibrillation (AF)

Definition

- **First diagnosed:** AF not diagnosed before, irrespective of its duration or the presence/ severity of AF-related symptoms.
- **Paroxysmal AF:** AF that terminates spontaneously or with intervention within 7 d of onset.
- **Persistent AF:** Continuous AF that is sustained >7 d.
- **Long-standing persistent AF:** Continuous AF >12 months in duration.
- **Permanent AF:** The term "permanent AF" is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm

Clinical presentation of AF

- **Asymptmatic AF:** Patient without symptoms and diagnosed with 12 leads ECG
- **Symptomatic AF:** Palpitation, dyspnea, fatigue, chest tightness, poor effort tolerance, and disordered sleep
- **Hemodynamically unstable:** Hypotension, heart failure, pulmonary edema, and myocardial ischemia

Evaluation of Patient of AF

- History and physical examination to define the onset of the first discovery of AF
- ECG to confirm rhythm, and identify LVH, prior MI, and presence of preexcitation
- Transthoracic ECHO: to identify LA, and RA size; LV and RV size and function; RV pressure; LA thrombus, and pericardial disease
- Blood test: Thyroid, renal, and hepatic function

Assessment of risk of stroke

- CHA2DS2-VASc score is recommended to assess stroke risk (Table 47 -1)
  - » CHA2DS2-VASc ≥ 1 in male and ≥ 2 female is considered at high risk of stroke and will need anticoagulation

Assessment of bleeding risk

- HAS-BLED score is used to identify patients at high risk of bleeding. (Table 47 -1)
- HAS-BLED ≥ 3 denotes high risk of bleeding
- High risk of bleeding should not lead to withholding anticoagulation
- HAS-BLED can be used to modify dose of oral anticoagulant in patients with concomitant antiplatelet therapy

Table 47-1: Bleeding and thrombotic risks

CHA2DS2-VASC		HAS-BLED	
Age ≥ 75 years	2	**Hypertension**	1
Age 65-74 years	1	**Abnormal liver or renal function**	1
History of congestive heart failure	1	**History of stroke/TIA**	1
History of stroke/TIA	2	**Bleeding history**	1
Hypertension	1	**Labile INR**	1
Vascular disease	1	**Age > 65 years**	1
Female sex	1	**Drug (NSAID)/ Excessive alcohol**	1

Management of AF

- Management of AF follows the integrated approach of
  - Assesmsent of risk of stroke
  - Clinical presentation
  - Duration of AF
- Management of AF should include two main pathways
  - Rate control versus rhythm control. Figure 47 -1
  - Prevention of stroke.Figure 47 -2

Rate control versus rhythm control

- Rate control is defined as heart rate < 110 b/min
- Rhythm control is defined as restoration of normal sinus rhythm
- Electric cardioversion is indicated in all patients presenting with AF and hemodynamic instability
- In patients with AF, the choice between rate control and rhythm control depends on patient symptoms and quality of life
  - Rhythm control is recommended for
    - Hemodynamically unstable patient
    - Patients with symptoms that decrease the quality of life.

Rhythm control in patients with AF

Restoration of normal sinus rhythm

- Restoring the normal rhythm is an integral part of management of patients with new onset AF
- Two methods for cardioversion

A. Synchronized Electrical cardioversion

- Indications
  - All patients with AF or atrial flutter and hemodynamic instability
  - Failure of pharmacological therapy to control rapid ventricular response rate with ongoing myocardial ischemia or HF
  - Selected patients with persistent AF
- Paddle position
  - Anterolateral position: single paddle is placed on the left fourth or fifth intercostal space on the midaxillary line; the other paddle is placed just to the right of the sternal edge on the second or third intercostal space.
  - Anteroposterior position: A single paddle is placed to the right of the sternum, as above, and the other paddle is placed between the tip of the left scapula and the spine
- Anteroposterior position is mor# effective than anterolateral position
- Joules
  - For AF Biphasic synchronized cardioversion 120-150 Joules
  - For atrial flutter synchronized cardioversion 70-120 Joules
- Pre-treatment with amiodarone, flecainide, or propafenone should be considered to facilitate the success of electrical cardioversion

B. Pharmacological cardioversion

- Pharmacological cardioversion of AF is indicated only in a hemodynamically stable patient, after consideration of thethrombo-embolic risk.
- Flecainide and propafenone are effective for cardioversion of AF in patients with no structural heart disease
- Vernakalant and amiodarone can be used in patient with mild heart failure (class I or II).
- Only IV amiodarone can be used in patients with LVEF < 40% or patients with significant aortic stenosis.
- Drugs used for rhythm control are shown in Table 47 -2

Table 47-2:Drugs used for rhythm control in patients with AF

Drug	Route	1st dose	Further dose	Precautious
Flecainide	**Oral (IV)**	**200-300 mg 2 mg/kg over 10 min**		**Should not be used in ischemic heart disease or structure heart disease Do not use in atrial flutter**
Propafenone	**Oral (IV)**	**450-600 mg 1-2 mg/kg over 10 min**		
Amiodarone	**IV**	**5-7 mg/kg over 1-2 h**	**50 mg/hr maximum 1.2 g for 24 hrs**	**Better to be in large peripheral vein or central vein**
Ibutilitide	**IV**	**1 mg over 10 min 0.01 mg/kg if body weight < 60 kg**	**1 mg over 10 min (10-20 min after the initial dose)**	**Can be used in atrial flutter Not used in patient with prolonged QT**

Maintenance of normal sinus rhythm

- Amiodarone is recommended for long-term rhythm control in all AF patients
- Flecainide or propafenone is recommended for long-term rhythm control in AF patients with normal LV function and without structural heart disease
- Sotalol may be considered for long-term rhythm control in patients with normal LV function

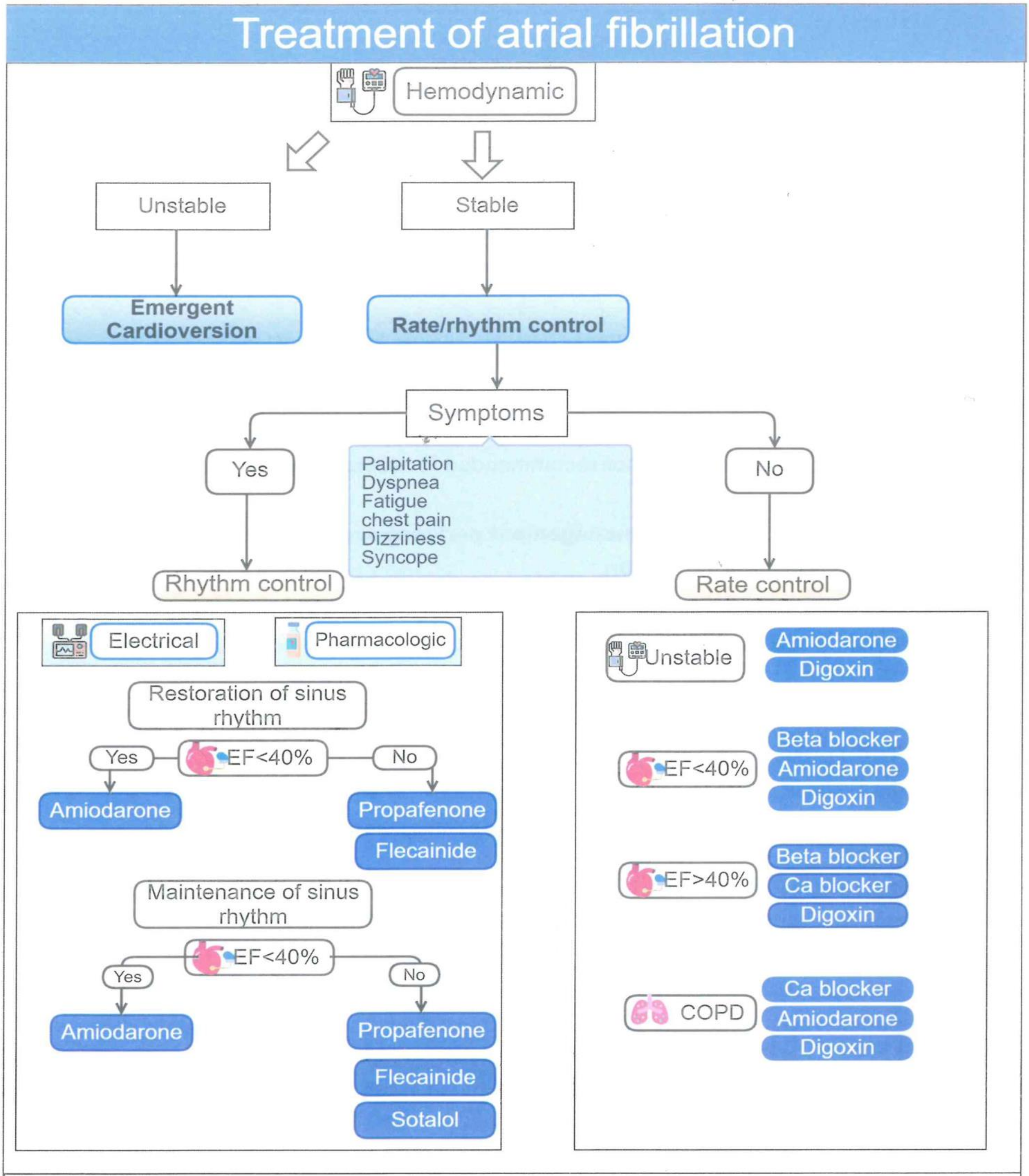
Rate control in patient with AF

- The choice of the drugs depends on patient characteristics, LVEF, and hemodynamics
- In patients with hemodynamic instability or severely depressed LVEF, intravenous amiodarone may be considered for acute control of heart rate
- Beta-blockers, diltiazem, or verapamil are recommended as first-choice drugs to control heart rate in AF patients with LVEF≥40%
- Beta-blockers and/or digoxin are recommended to control heart rate in AF patients with EF<40%
- Diltiazem, verapamil and/or digoxin are recommended to control heart rate in AF patient with severe asthma or chronic obstructive pulmonary disease.
- In patients with pre-excitation and AF, digoxin, non-dihydropyridine calcium channel antagonists Beta blockers, or intravenous amiodarone should not be administered as they may increase the ventricular response and may result in ventricular fibrillation
- Drugs used for rate control are shown in Table 47 -3

Table 47-3:Drug used for rate control in patients with AF

Drug	Intravenous	Oral	Precautious
Beta blockers			
Metoprolol	Oral (IV)	200-300 mg 2 mg/kg over 10 min	Should not be used in ischemic heart disease or structure heart disease Do not use in atrial flutter
Bisprolol	Oral (IV)	450-600 mg 1-2 mg/kg over 10 min	
Atenolol	IV	5-7 mg/kg over 1-2 h	Better to be in large peripheral vein or central vein
Carvidolol	IV	1 mg over 10 min 0.01 mg/kg if body weight < 60 kg	Can be used in atrial flutter Not used in patient with prolonged QT
Calcium channel blocker			
Verapamil	2.5 - 10 mg i.v. bolus over 5 min	40 mg b.i.d. to 480 mg (extended release) o.d.	Contraindicated in heart failure with reduced ejection fraction
Diltiazem	0.25 mg/kg i.v. bolus over 5 min, then 5-15 mg/h	60 mg t.i.d. to 360 mg (extended release) o.d.	
Digitalis			
Digoxin	0.5 mg i.v. bolus (0.75 - 1.5 mg over 24 hours in divided doses)	0.0625 - 0.25 mg o.d.	High plasma levels associated with increased mortality Check renal function before starting and adapt dose in CKD patients

Other			
Amiodarone	300 mg i.v. diluted in 250 mL 5% dextrose over 30 - 60 min (preferably via central venous cannula), followed by 900 - 1200 mg i.v. over 24 hours diluted in 500 - 1000 mL via a central venous cannula	200 mg o.d. after loading 3 x 200 mg daily over 4 weeks, then 200 mg daily	In case of thyroid disease, only if no other options


Treatment of atrial fibrillation
Hemodynamic
Unstable
Stable
Emergent Cardioversion
Rate/rhythm control
Symptoms
Yes
No
Palpitation
Dyspnea
Fatigue
chest pain
Dizziness
Syncope
Rhythm control
Rate control
Electrical
Pharmacologic
Restoration of sinus rhythm
Yes
EF<40%
No
Amiodarone
Propafenone
Flecainide
Maintenance of sinus rhythm
EF<40%
Yes
No
Amiodarone
Propafenone
Flecainide
Sotalol
Unstable
Amiodarone
Digoxin
EF<40%
Beta blocker
Amiodarone
Digoxin
EF>40%
Beta blocker
Ca blocker
Digoxin
COPD
Ca blocker
Amiodarone
Digoxin

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS):Eur Heart J 2021; 42:373-498

Figure 47-1:Rate/rhythm control management guideline

Prevention of stroke

Recommendation for stroke risk management without cardioversion

- In AF patients with mechanical valve or with moderate to severe mitral stenosis. Vitamin K antagonists (VKAs)
- In AF patients with low risk of stroke, (CHA2DS2-VASc score = 0 in men, or 1 in women), antitherapeutic therapy is not required
- In AF patients with high risk of stroke (CFIA2DS2-VASc score = 3 in men, or 2 in women), antitherapeutic therapy is recommended
- In AF patients with CHA2DS2-VASc score = 2 in men, or 1 in women), antitherapeutic therapy should be considered
- For stroke prevention in AF patients who are eligible for oral anticoagulants. New oral anticoagulants (NOAC) are recommended in preference to VKAs (excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis)
- If a VKA is used, a target INR of 2.0 - 3.0 is recommended.
- Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk

Recommendation for stroke risk management pericardioversion

Anitcogulation before cardioversion

Hemodynamically unstable patients

- Emergency cardioversion using synchronized direct current electrical cardioversion.

Hemodynamically stable patient on therapeutic oral anticoagulation

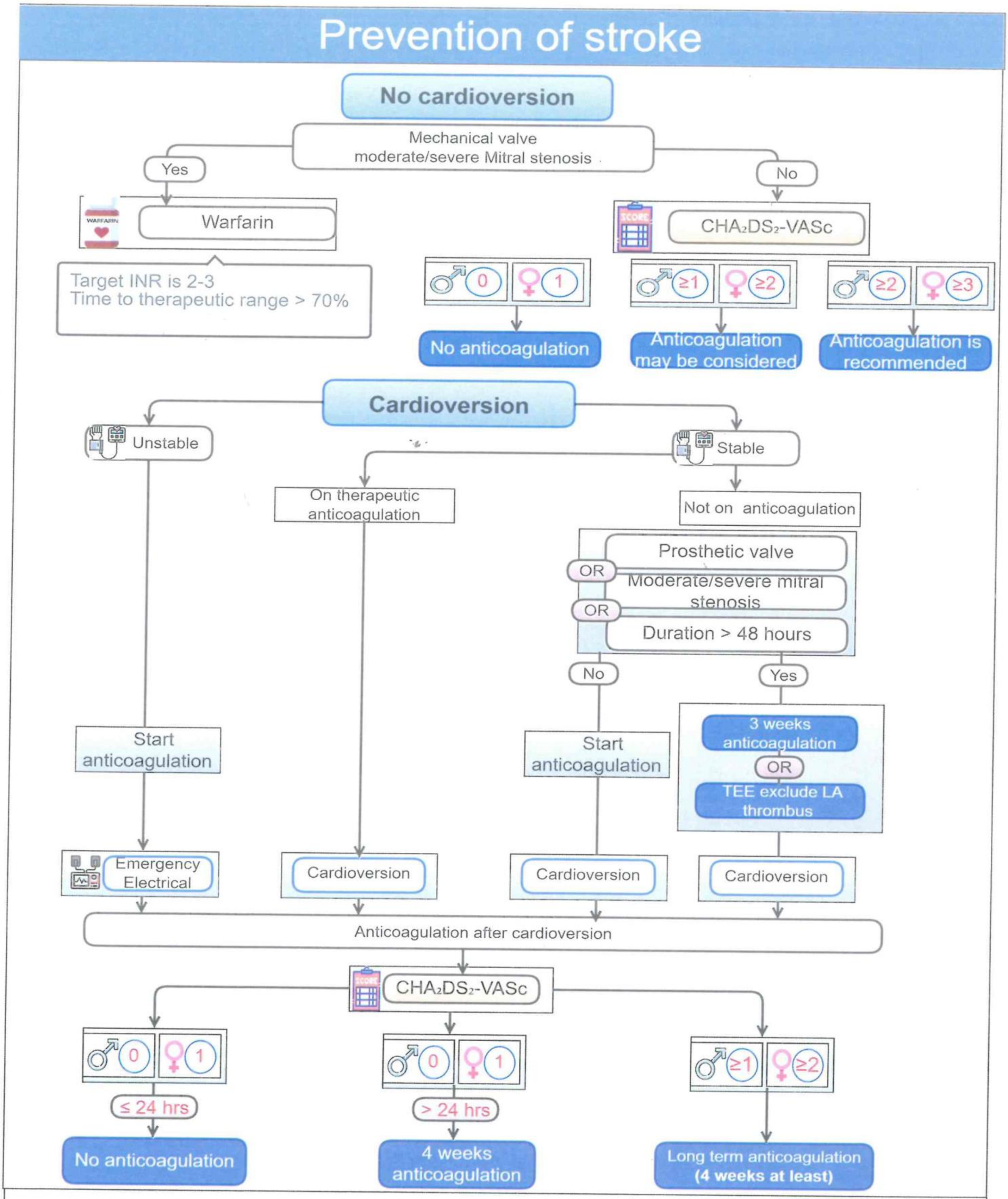
- For AF patients who are already on therapeutic oral anticoagulation, cardioversion can be done either immediately or elective

Hemodynamically stable patient not on therapeutic oral anticoagulation

- Cardioversion is guided by risk of thromboembolic event
- AF patient at high risk of thromboembolic event, cardioversion should be planned after appropriate anticoagulation therapy.
- Appropriate anticoagulation therapy includes two regimens
  - 3 weeks preprocedural therapeutic anticoagulation or
  - Transesophageal echocardiography to exclude LA thrombus
- AF patients are considered at high risk of thromboembolism if any of following factor is present
  - AF duration > 48 hours or of unknown time of onset
  - Prothetic valve
  - Moderate, severe mitral stenosis
  - History of thromboembolism
- Immediate cardioversion can be offered to AF patients at low risk of thromboembolic event (AF duration < 48 hours AND no other risk factors)

Anticoagulation after cardioversion

- In patients with a definite duration of AF ≤24 h and a very low stroke risk (CHA2DS2-VASc score of 0 in men or 1 in women] post-cardioversion anti-coagulation for 4 weeks may be omitted
- In patients with AF duration of >24 h undergoing cardioversion, therapeutic anticoagulation should be continued for at least 4 weeks


Prevention of stroke
No cardioversion
Mechanical valve
moderate/severe Mitral stenosis
Yes
No
WARFARIN
Warfarin
Target INR is 2-3
Time to therapeutic range > 70%
SCORE
CHA2DS2-VASc
♂ 0 ♀ 1
No anticoagulation
♂ ≥1 ♀ ≥2
Anticoagulation may be considered
♂ ≥2 ♀ ≥3
Anticoagulation is recommended
Cardioversion
Unstable
Stable
On therapeutic anticoagulation
Not on anticoagulation
Prosthetic valve
OR
Moderate/severe mitral stenosis
OR
Duration > 48 hours
No
Yes
Start anticoagulation
Start anticoagulation
3 weeks anticoagulation
OR
TEE exclude LA thrombus
Emergency Electrical
Cardioversion
Cardioversion
Cardioversion
Anticoagulation after cardioversion
SCORE
CHA2DS2-VASc
♂ 0 ♀ 1
≤ 24 hrs
No anticoagulation
♂ 0 ♀ 1
> 24 hrs
4 weeks anticoagulation
♂ ≥1 ♀ ≥2
Long term anticoagulation
(4 weeks at least)

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS):Eur Heart J 2021; 42:373-498

Figure 47-2:Primary stroke prevention in patient with AF

Management of patient presenting with AF in special population

Patient with AF and acute coronary syndrome, PCI, and chronic coronary syndrome

- In AF patients eligible for NOACs, it is recommended to use a NOAC in preference to a VKA in combination with antiplatelet therapy
- In patients at high bleeding risk (HAS-BLED ≥3), rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk
- In patients at high bleeding risk (HAS-BLED ≥3), dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.
- Management of AF in special population is described in Figure 47-3

Acute coronary syndrome (ACS) and PCI

- In AF patients with ACS undergoing an uncomplicated PCI, triple therapy with aspirin, clopidogrel, and an OAC for longer than 1 week after an ACS should be considered with the total duration (≤1 month)
- Continuation of dual therapy with an OAC and a P2Y 12 inhibitor (preferably clopidogrel) for up to 12 months is recommended

Chronic coronary syndrome (CCS) and PCI

- In AF patients with CCS undergoing an uncomplicated PCI, triple therapy with aspirin, clopidogrel, and an OAC for longer than 1 week after an ACS should be considered with the total duration (≤1 month)
- Continuation of dual therapy with an OAC and a P2Y 12 inhibitor (preferably clopidogrel) for up to 6 months is recommended

Medically treated ACS

- Dual therapy with an OAC and a P2Y 12 inhibitor (preferably clopidogrel) for up to 6 months is recommended.

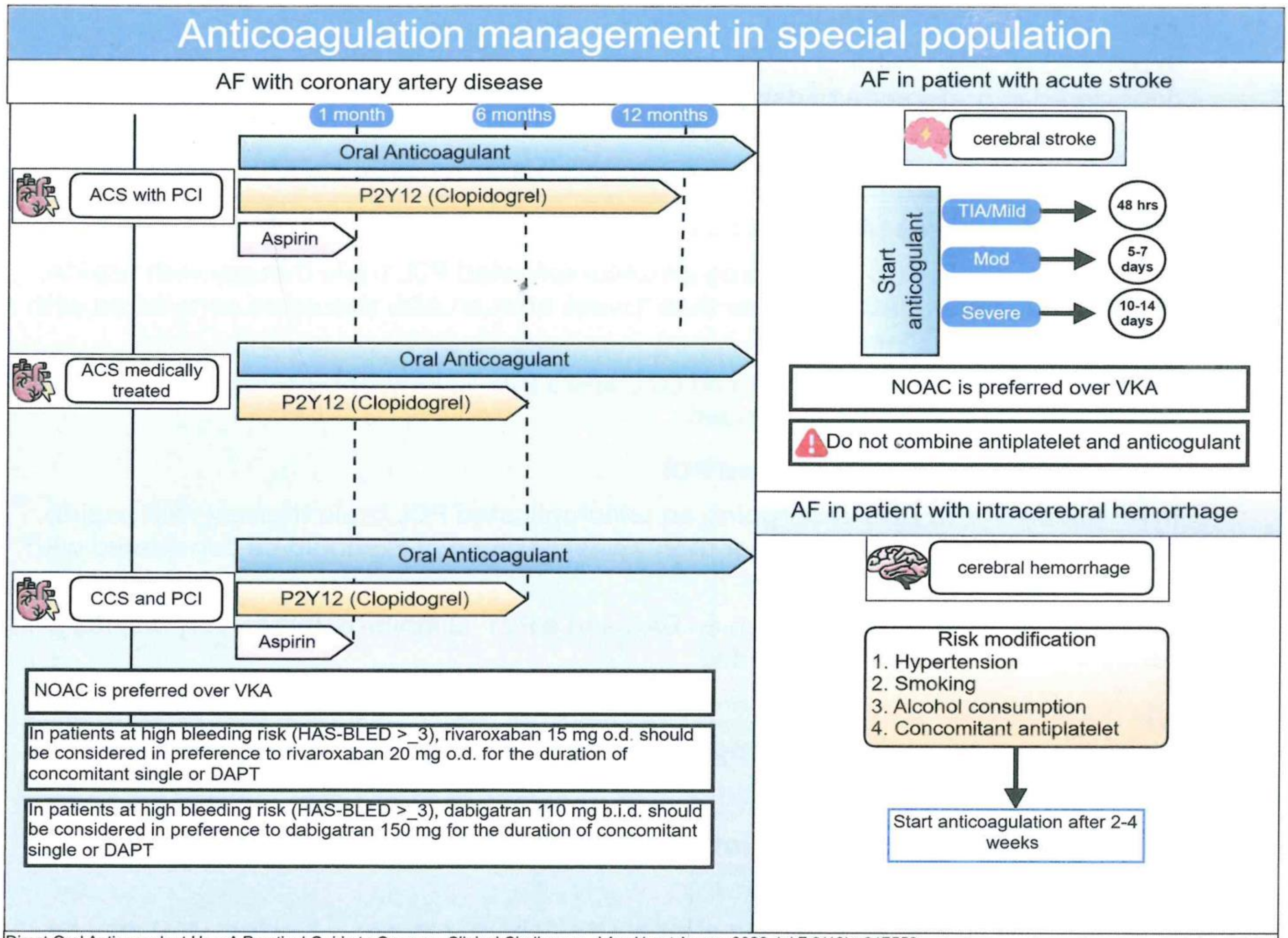
Patient with AF and acute stroke or intracranial hemorrhage

Patients with AF and acute stroke

- Optimal timing of anticoagulation after acute ischemic stroke is lacking, OAC may be initiated 4-14 after acute event
- There is no evidence that the addition of aspirin to OAC or supratherapeutic INRs would improve outcomes in secondary stroke prevention.
- Compared with VKAs, NOACs were associated with better efficacy in secondary stroke prevention and better safety regarding ICH
- In AF patients presenting with acute ischemic stroke, very early anticoagulation (<48 h) using UFH, LMWH, or VKAs is not recommended

Patients with AF and intracranial hemorrhage

- In AF patients at high risk of ischemic stroke, re-initiation of OAC, with preference for NOACs over VKAs in NOAC-eligible patients, should be considered in consultation with a neurologist/stroke specialist after:
  - » A trauma-related ICH
  - » Acute spontaneous ICH


Anticoagulation management in special population
AF with coronary artery disease
1 month
6 months
12 months
Oral Anticoagulant
ACS with PCI
P2Y12 (Clopidogrel)
Aspirin
Oral Anticoagulant
ACS medically treated
P2Y12 (Clopidogrel)
Oral Anticoagulant
CCS and PCI
P2Y12 (Clopidogrel)
Aspirin
AF in patient with acute stroke
cerebral stroke
Start anticoagulant
TIA/Mild
48 hrs
Mod
5-7 days
Severe
10-14 days
AF in patient with intracerebral hemorrhage
cerebral hemorrhage
Start anticoagulation after 2-4 weeks

NOAC is preferred over VKA

In patients at high bleeding risk (HAS-BLED >_3), rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT

In patients at high bleeding risk (HAS-BLED >_3), dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg for the duration of concomitant single or DAPT

NOAC is preferred over VKA

Do not combine antiplatelet and anticoagulant

Risk modification
1. Hypertension
2. Smoking
3. Alcohol consumption
4. Concomitant antiplatelet

Direct Oral Anticoagulant Use: A Practical Guide to Common Clinical Challenges. J Am Heart Assoc. 2020 Jul 7;9(13):e017559
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS):Eur Heart J 2021; 42:373-498
AF: atria fibrillation, ACS: acute coronary syndrome, CCS: chronic coronary syndrome: PCI: percutaneous coronary intervention, NOAC: New oral anticoagulant, VKA: vitamin K antagonsit, TIA: transient ischemic attack

Figure 47-3: Anticoagulation management of AF in special population

References

1. Hindricks G. Potpara T, Dagres N, et al. ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42:373-498..
2. January CT, Wann LS, Alpert JS, et al.2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014 Dec 2;64(21):e1-76
3. January CT, Wann LS, CalkinH et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. Circulation 2019, 140:-e125e151

Chapter 48

Acute coronary syndrome

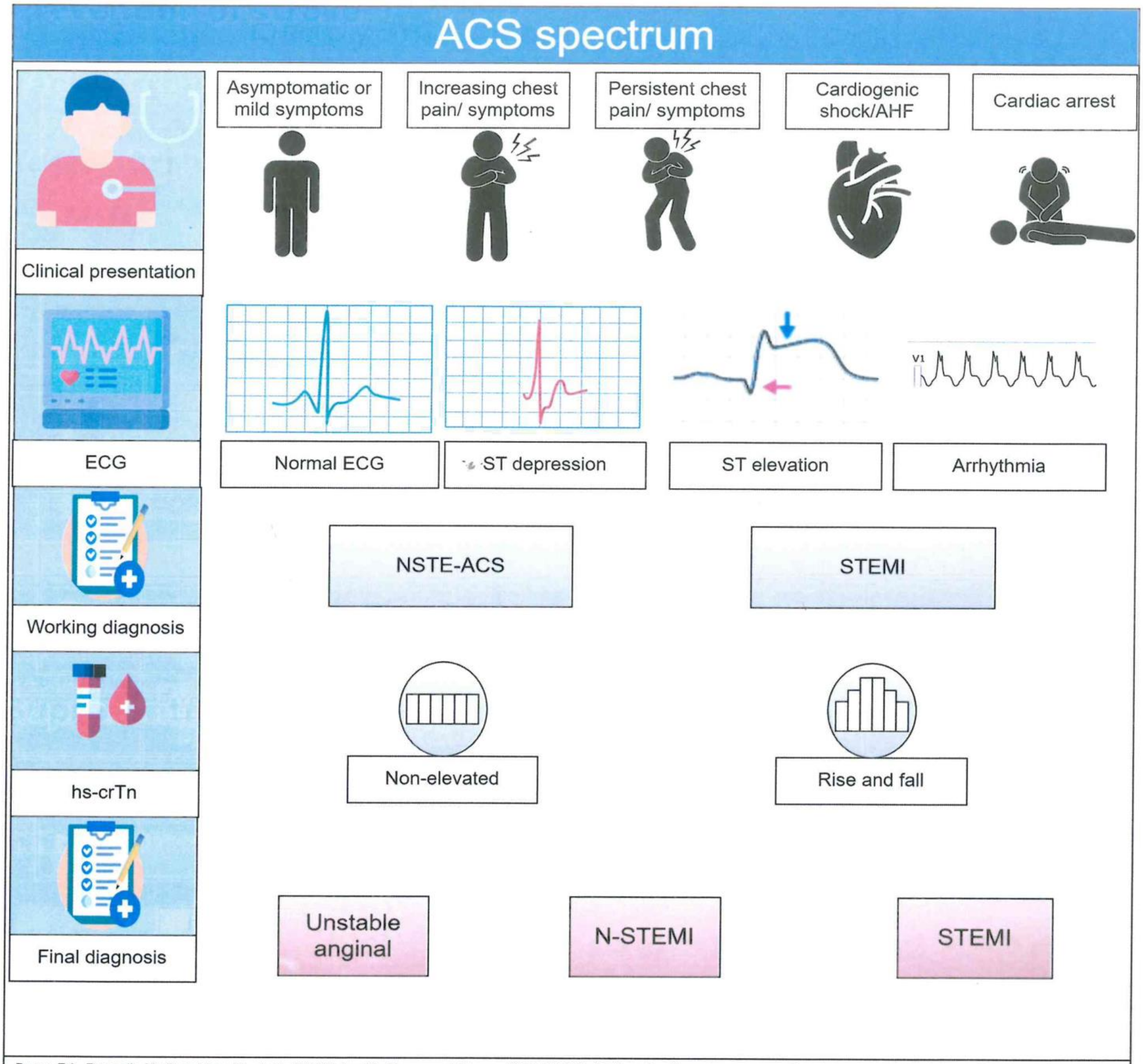
Definitions

- Acute coronary syndrome (ACS] encompasses a spectrum of conditions that include patients presenting with recent changes in clinical symptoms or signs, with or without changes on 12-lead electrocardiogram (ECG) and with or without acute elevations in cardiac troponin (cTn) concentrations. (Figure 48 1]
- Patients presenting with suspected ACS may eventually receive a diagnosis of acute myocardial infarction (AMI) or unstable angina (UA)
- The diagnosis of myocardial infarction (MI) is associated with cTn release and is made based on the fourth universal definition of MI.
  - » Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the followings
    - Symptoms of myocardial ischemia
    - New ischemic ECG changes
    - Development of pathological Q waves
    - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology
    - Identification of a coronary thrombus by angiography or autopsy
- Myocardial injury is another distinct entity, used to describe troponin release due to mechanisms other than myocardial ischemia and not meeting the criteria for MI outlined above.
- Unstable angina is defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis. It is characterized by specific clinical findings:
  - » Prolonged (>20 min) angina at rest;
  - » New onset of severe angina;
  - » Angina that is increasing in frequency,
  - » Longer in duration, or lower in threshold; or
  - » angina that occurs after a recent episode of MI.

Types of Myocardial Infarction

- Type 1: (spontaneous MI): Related to atherosclerotic plaque rupture
- Type 2: (MI secondary to an ischemic imbalance): MI consequent to increased oxygen demand or a decreased supply e.g. anemia, tachyarrhythmia, and coronary spasm
- Type 3: MI resulting in death when biomarker values are unavailable): Sudden, unexpected cardiac death before blood samples for biomarkers could be drawn or before their appearance in the circulation.
- Type 4a: (MI related to percutaneous coronary intervention [PCI]): Elevation of biomarker values (cTn is preferred) to more than 5 times the 99 th percentile of the URL in patients with normal baseline values

- Type 4b (MI related to stent thrombosis): MI associated with stent thrombosis as detected by coronary angiography or autopsy in the setting of myocardial ischemia in combination with a rise and/or fall of cardiac biomarkers with at least one value above the 99 th percentile URL
- Type 5 (MI related to coronary artery bypass grafting [CABG]): Elevation of cardiac biomarker values more than 10 times the 99 th percentile URL in patients with normal baseline cTn values. In addition, either
    - » New pathologic Q waves or new BBB,
    - » Angiographic-documented new graft or native coronary artery occlusion, or
    - » Evidence of new loss of viable myocardium or new regional wall motion abnormality by cardiac imaging is required.


ACS spectrum
Clinical presentation
Asymptomatic or mild symptoms
Increasing chest pain/ symptoms
Persistent chest pain/ symptoms
Cardiogenic shock/AHF
Cardiac arrest
ECG
V1
Normal ECG
ST depression
ST elevation
Arrhythmia
Working diagnosis
NSTE-ACS
STEMI
hs-crTn
Non-elevated
Rise and fall
Final diagnosis
Unstable anginal
N-STEMI
STEMI

Byrne RA, Rossello X, Coughlan JJ, et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J Acute Cardiovasc Care. 2023 Sep 22:zuad107

ACS, acute coronary syndrome; ECG, electrocardiogram; AHF: acute heart failure; hs-cTn, high-sensitivity cardiac troponin; NSTE-ACS, non-ST-elevation acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction

Figure 48-1: Spectrum of acute coronary syndrome

Evaluation of patients presented with symptoms suggesting acute coronary syndrome

Physical examination

Chest pain

- Retrosternal sensation of pain, pressure, or heaviness ('angina') radiating to the left arm, both arms, the right arm, the neck, or the jaw, which may be intermittent (usually lasting several minutes) or persistent

  - Additional symptoms: sweating, nausea, vomiting, epigastric pain, dyspnea, and syncope

Hemodynamic instability

- In patients presenting with cardiac arrest or hemodynamic instability of presumed cardiovascular origin, echocardiography should be performed/interpreted by trained physicians immediately following a 12-lead ECG.

ECG criteria

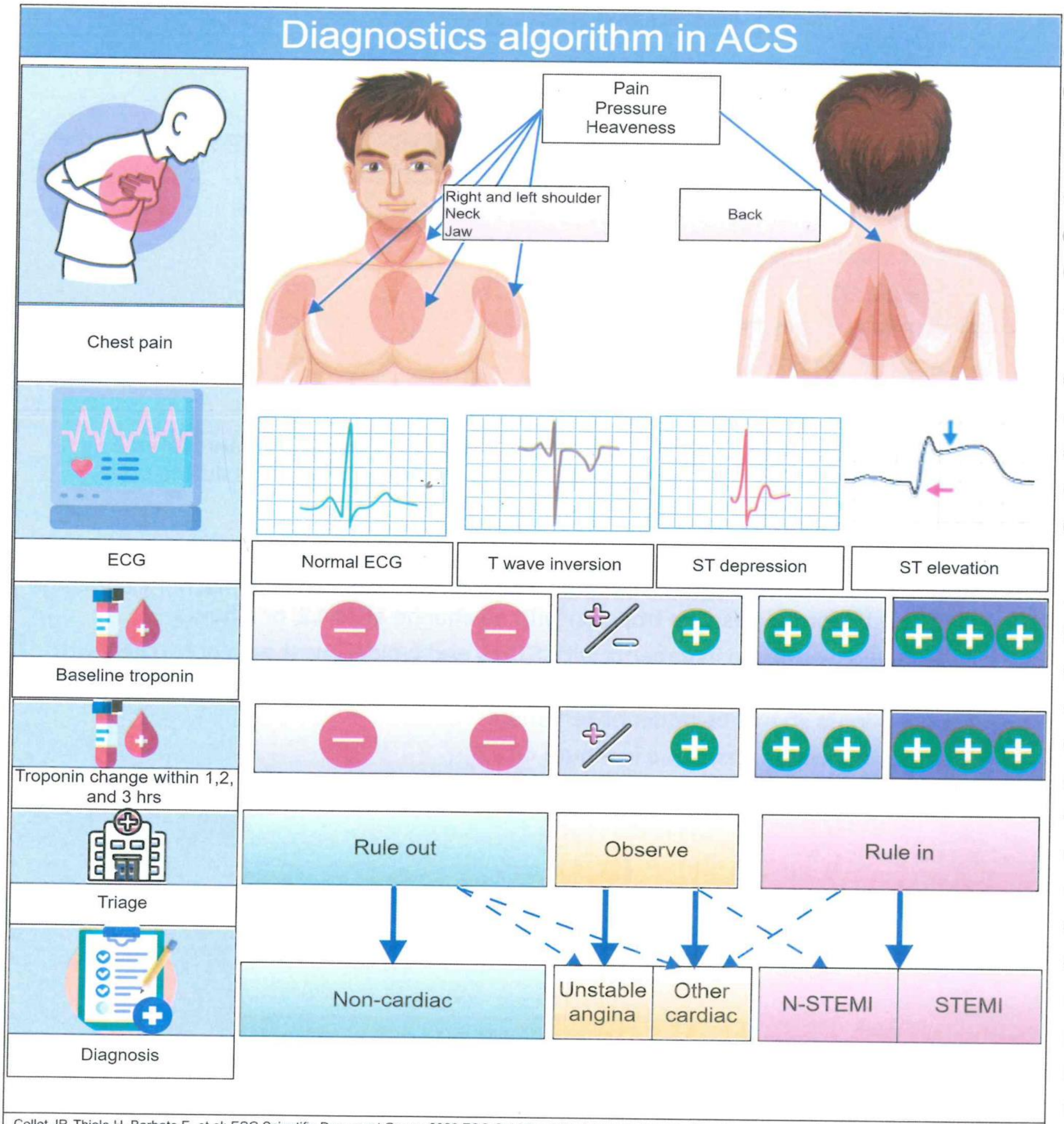
- Patient may be presented with either
  - Normal ECG
  - ECG criteria of STEMI
  - ECG criteria of Non-STEMI

Biomarkers

- Cardiac troponin and its change during serial sampling should be interpreted as a quantitative marker: the higher the 0 h level or the absolute change during serial sampling, the higher the likelihood for the presence of MI.

Triage

- ACS can be ruled out in stable patients who are presented with normal or mild change in ECG with normal baseline troponin with no change after 1,2, or 3 hours
- ACS should be ruled in in patients with STEMI and typical chest pain or NSTEMI with either high baseline troponin and/or significant change in troponin
- Other patients should be under observation.
- Triaging pathway is described in Figure 48 -2


Diagnostics algorithm in ACS
Pain
Pressure
Heaveness
Right and left shoulder
Neck
Jaw
Back
Chest pain
ECG
Normal ECG
T wave inversion
ST depression
ST elevation
Baseline troponin
Troponin change within 1,2, and 3 hrs
Triage
Rule out
Observe
Rule in
Diagnosis
Non-cardiac
Unstable angina
Other cardiac
N-STEMI
STEMI

Collet JP, Thiele H, Barbato E, et al; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42:1289-1367
STEMI: ST-segment elevation myocardial infarction

Figure 48-2: Diagnostic algorithm and triage in acute coronary syndrome

Other causes of acute chest pain that mimic ACS

- The following table list the most important causes of acute chest pain that mimic ACS

Table 48-1: Differential diagnoses of acute coronary Syndrome

Cardiac	Pulmonary	Vascular	GIT	Orthopedics	Others
Myocarditis Cardiomyopathy Heart failure Tachycardia Hypertensive emergencies Takotsubo cardiomyopathy Coronary spasm	Pulmonay embolism Tension pneumothorax	Aortic dissection	Esophageal spasm	Chest trauma Muscle injury	Anexiety disorder

ST-segment elevation myocardial infarction (STEMI)

Diagnostic Criteria

- Persistent chest discomfort or other symptoms suggestive of ischemia and ST-segment elevation in at least two contiguous leads

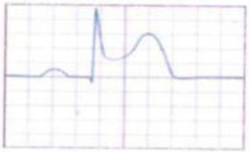
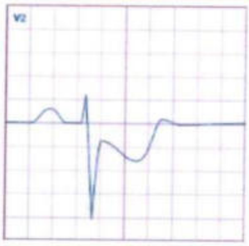
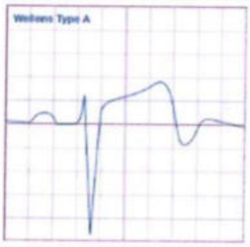
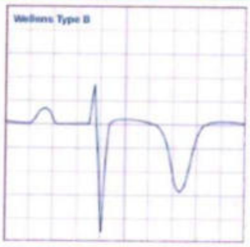
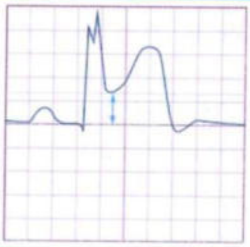
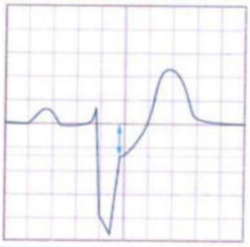
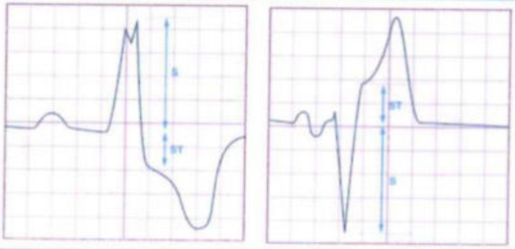
Chest Pain

- Symptoms of MI: central crushing chest pain, usually severe, persisting for 15 minutes or more. Often accompanied by sweating; nausea, belching or vomiting.

ECG Criteria of STEMI And STEMI Equivalent Diagnosis

- ST elevation > 1 mm in at least 2 contagious anatomical leads except V2-3.
- In V2-V3, ST elevation ≥ 2.5 mm in male < 40 years and ≥ 2.0 mm in male ≥ 40 years. In female ST elevation ≥ 1.5 mm at any age
- ST-segment depression in leads V 1 -V 3 suggests myocardial ischemia, especially when the terminal T-wave is positive (ST-segment elevation equivalent), and confirmation by concomitant ST-segment elevation ≥ 0.5 mm recorded in leads V 7 -V 9 should be considered as a means to identify posterior MI
- Diagnosis of myocardial ischemia in patient with left bundle branch block is presented in Table 48 -2
- Ventricular pacemaker prevents interpretation of ST segment and patient may require urgent angiography
- Ischemia of left main may present with atypical ECG" ST depression ≥ 1 mm in eight or more surface leads e.g. inferolateral wit ST elevation aVR and/or V1

Table 48-2; ECG patterns in STEMI

ST elevation	**ST elevation > 1 mm in at least 2 contagious anatomical leads except V2-3. InV2-V3, ST elevation ≥ 2.5 mm in male < 40 years and ≥ 2.0 mm in male ≥ 40 years. In female ST elevation ≥ 1.5 mm at any age**	
Posterior STEMI	**ST-segment depression in leads V 1 -V 3 suggests myocardial ischemia, especially when the terminal T-wave is positive (ST-segment elevation equivalent), and confirmation by concomitant ST-segment elevation ≥ 0.5 mm recorded in leads V 7 -V 9 should be considered as a means to identify ppsterior MI**	
LAD critical stenosis (Wellens sign)	**Wellens type A: Biphasic T waves with the initial deflection positive and the terminal deflection negative**	
	Wellens type B: T-waves are deeply and symmetrically inverted	
STEMI in LBBB or pace maker	**Concordant ST-segment elevation ≥ 1mm in any lead**	
	Concordant ST-segment depression ≥ 1mm in V1-V3	
	Discordant ST-segment: ST:S ratio ≥ 0.25 in any lead	

STEMI clinical pathway

- STEMI pathway is described in Figure 48 -3

Patient with onset of symptoms < 12 hours

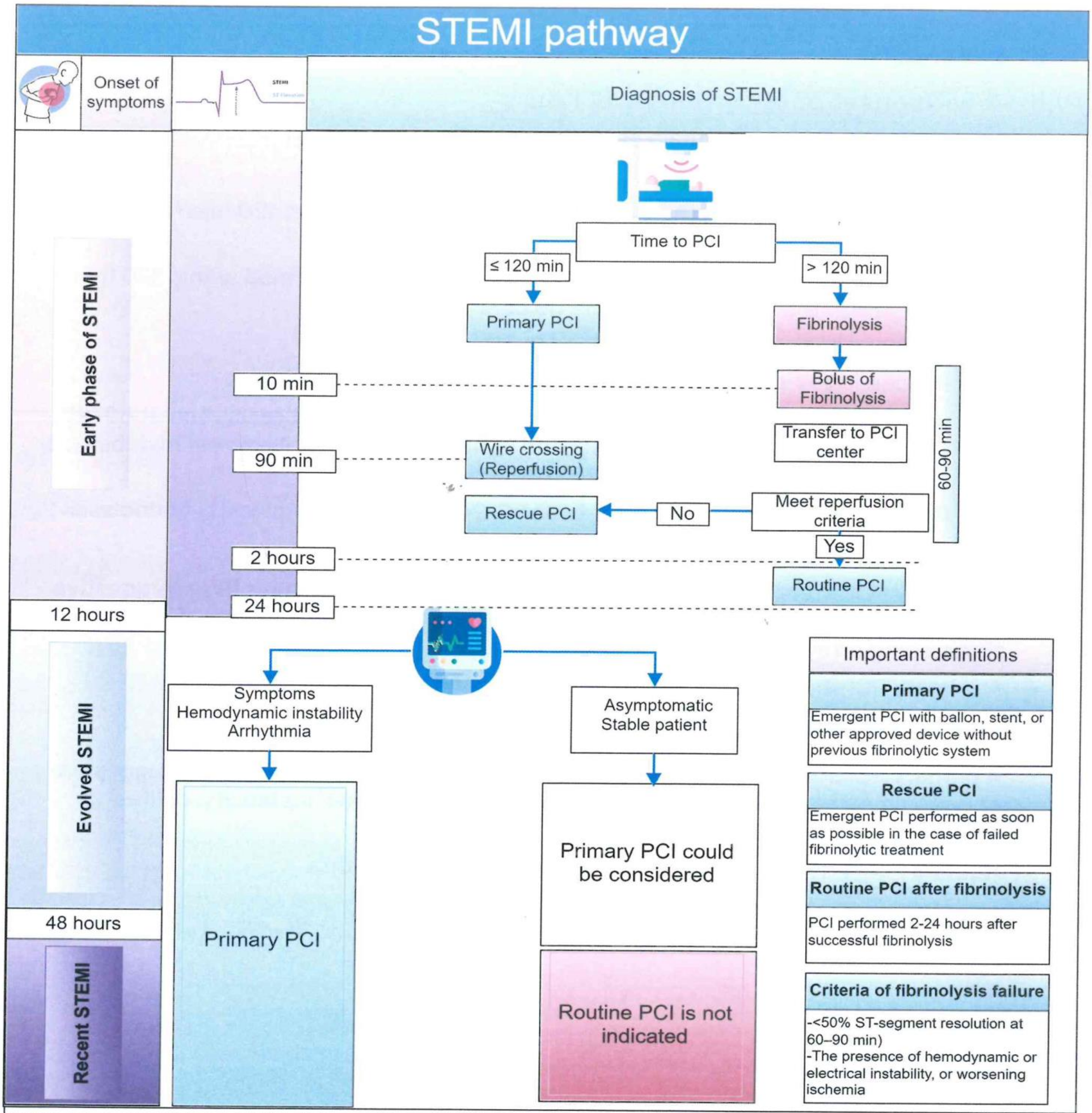
- Reperfusion therapy is the main stay of management.
- Reperfusion strategies include
    - » Primary PCI is preferred therapy if it can be performed within 120 min from STEMI diagnosis
    - » Fibrinolysis is recommended if primary PCI cannot be performed within 120 min from STEMI diagnosis and there are no contraindication.
        - The dose of fibrinolysis is described in Table 48 -3
        - Rescue PCI is indicated immediately when fibrinolysis has failed.
            - › Criteria of fibrinolysis failure include (<50% ST-segment resolution at 60–90 min) or at any time in the presence of hemodynamic or electrical instability, or worsening ischemia.
        - Routine PCI is recommended between 2-24 hours after successful fibrinolysis

Patient with onset of symptoms 12-48 hours

- A primary PCI strategy is indicated in the presence of signs or symptoms suggestive of ongoing myocardial ischemia, heart failure, hemodynamic instability, or life-threatening arrhythmias.
- A primary PCI should be considered in stable asymptomatic patients.

Patient with onset of symptoms > 48 hours

- A primary PCI strategy is indicated in the presence of signs or symptoms suggestive of ongoing myocardial ischemia, heart failure, hemodynamic instability, or life-threatening arrhythmias
- Routine PCI is NOT indicated in stable asymptomatic patients


STEMI pathway
Onset of symptoms
STEMI
ST Elevation
Diagnosis of STEMI
Early phase of STEMI
Time to PCI
≤ 120 min
> 120 min
Primary PCI
Fibrinolysis
10 min
Bolus of Fibrinolysis
Transfer to PCI center
60-90 min
90 min
Wire crossing (Reperfusion)
Rescue PCI
No
Meet reperfusion criteria
Yes
2 hours
Routine PCI
24 hours
12 hours
Evolved STEMI
Symptoms Hemodynamic instability Arrhythmia
Asymptomatic Stable patient
Primary PCI
Primary PCI could be considered
48 hours
Recent STEMI
Routine PCI is not indicated

Important definitions

Primary PCI

Emergent PCI with ballon, stent, or other approved device without previous fibrinolytic system

Rescue PCI

Emergent PCI performed as soon as possible in the case of failed fibrinolytic treatment

Routine PCI after fibrinolysis

PCI performed 2-24 hours after successful fibrinolysis

Criteria of fibrinolysis failure

-<50% ST-segment resolution at 60–90 min)
-The presence of hemodynamic or electrical instability, or worsening ischemia

Ibanez B, James S, Agewall S, A. et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39:119-177

PCI:Percutaneous Coronary Intervention; STEMI: ST-segment elevation myocardial infarction

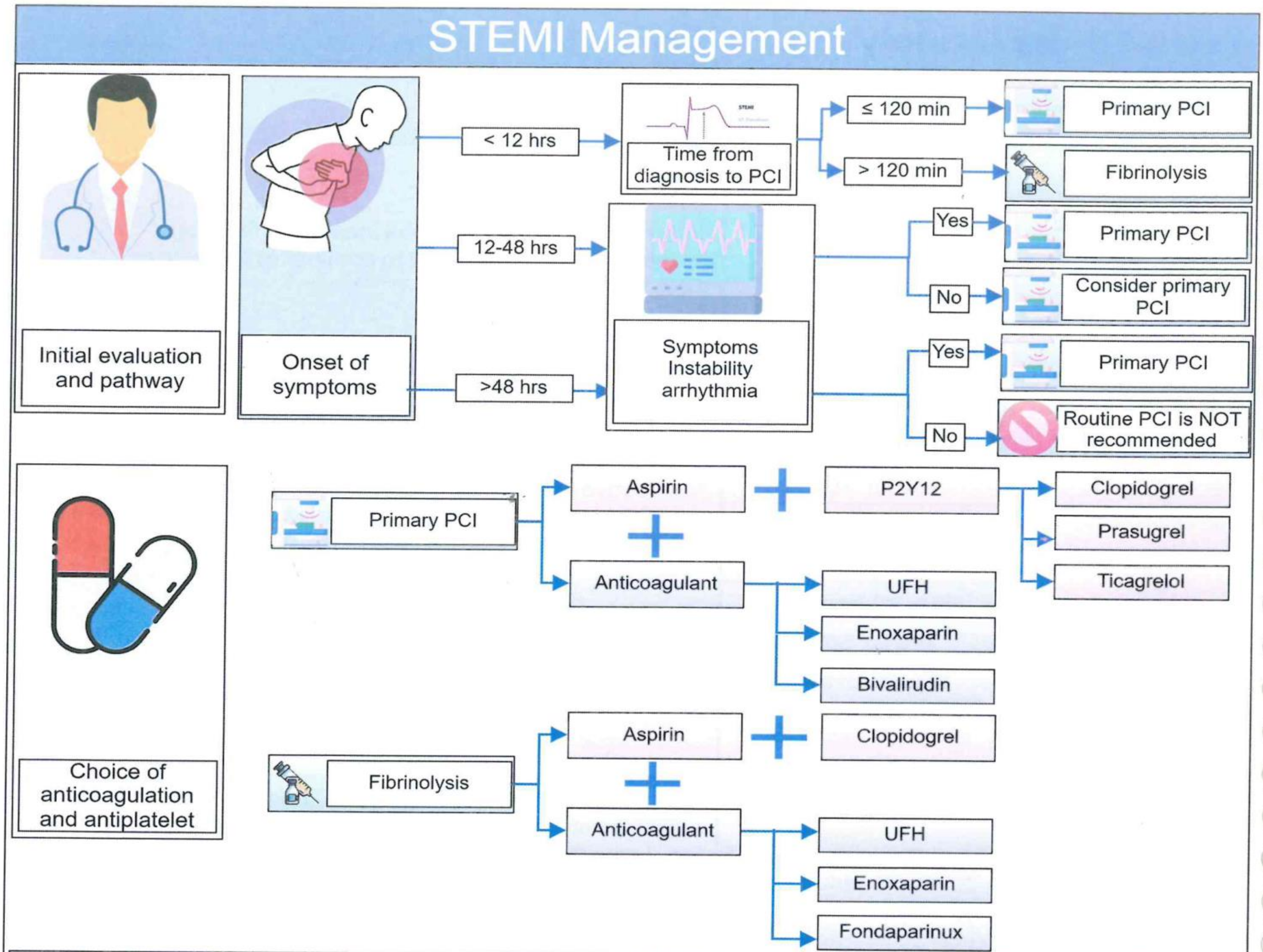
Figure 48-3: STEMI reperfusion pathway

Table 48-3: Fibrinolysis in STEMI

Drug	Recommended IV Regimen*	Advantages and Limitations
Alteplase (accelerated regimen)	15 mg bolus	Better outcomes than streptokinase; costlier than streptokinase; more difficult to administer because of short half-life
	then 0.75 mg/kg (maximum 50 mg) over 30 minutes	
	then 0.5 mg/kg (maximum 35 mg) over the next 60 minutes	
Tenecteplase	Single bolus over five to ten seconds based upon body weight:	As effective as alteplase with less noncerebral bleeding and need for transfusion; easier to administer (single bolus due to longer half-life) both in and out of hospital.
	<60 kg: 30 mg	
	60 to 69 kg: 35 mg	
	70 to 79 kg: 40 mg	
	80 to 89 kg: 45 mg	
	≥90 kg: 50 mg	
Reteplase	10 units over two minutes then repeat 10 unit bolus at 30 minutes	Similar outcomes as alteplase but easier to administer
Streptokinase	1.5 million units over 30 to 60 minutes	Generally a much less costly option than other fibrinolytics but outcomes are inferior. Neutralizing antibodies develop, which can diminish efficacy of subsequent use. Elevated risk of hypersensitivity reaction with repeated doses. Used extensively outside North America due to lower cost. (Not available in US or CAN).

STEMI periprocedural antithrombotic agents

- The periprocedural antithrombotic agents include antiplatelet and anticoagulants agents.
- The combination of anticoagulants and antiplatelets depends on whether the reperfusion will be done using PCI or fibrinolysis.
- The periprocedural regimen is described in Figure 48-4


STEMI Management
Initial evaluation and pathway
Onset of symptoms
< 12 hrs
Time from diagnosis to PCI
≤ 120 min
Primary PCI
> 120 min
Fibrinolysis
12-48 hrs
>48 hrs
Symptoms Instability arrhythmia
Yes
Primary PCI
No
Consider primary PCI
Yes
Primary PCI
No
Routine PCI is NOT recommended
Choice of anticoagulation and antiplatelet
Primary PCI
Aspirin
P2Y12
Clopidogrel
Prasugrel
Ticagrelol
Anticoagulant
UFH
Enoxaparin
Bivalirudin
Fibrinolysis
Aspirin
Clopidogrel
Anticoagulant
UFH
Enoxaparin
Fondaparinux

Primary PCI

Antiplatelets doses	Anticogaulant doses
Aspirin -Loading 150-300 mg orally -Maintenance: 75-100 mg orally	**Heparin** -bolus 70-100 IU/kg IV -50-70 IU/kg IV bolus with GP IIb/IIIa inhibitor
Clopidogrel -Loading 600 mg orally -Maintenance: 75 mg orally	**Enoxaparin** -0.5 mg/kg IV bolus
Prasugrel -Loading 60 mg orally -Maintenance: 10 mg orally	**Bivalirudin** -0.75 mg/kg IV bolus followed by 1.75 mg/kg/hr infusion up to 4 hrs after procedure
Ticagrelol -Loading 180 mg orally -Maintenance: 90 mg/12 hr orally	

Fibrinolysis

Antiplatelets doses	Anticogaulant doses
Aspirin -Loading 150-300 mg orally -Maintenance: 75-100 mg orally	**Heparin** -bolus 60 IU/kg IV followed by 12 IU/kg/hr with maximum 1000U/hr for 24-48 hrs
Clopidogrel -Loading 300 mg orally -Maintenance: 75 mg orally	**Enoxaparin** **Patient < 75 ys:** 30 mg IV bolus followed by 1 mg/kg sc/12 hrs **Patient ≥ 75 ys**: No IV bolus with first dose 0.75 mg/kg sc
	Fondaparinux (only with streptokinase) -Loading 2.5 mg IV followed by sc dose of 2.5 mg sc once daily up to 8 days

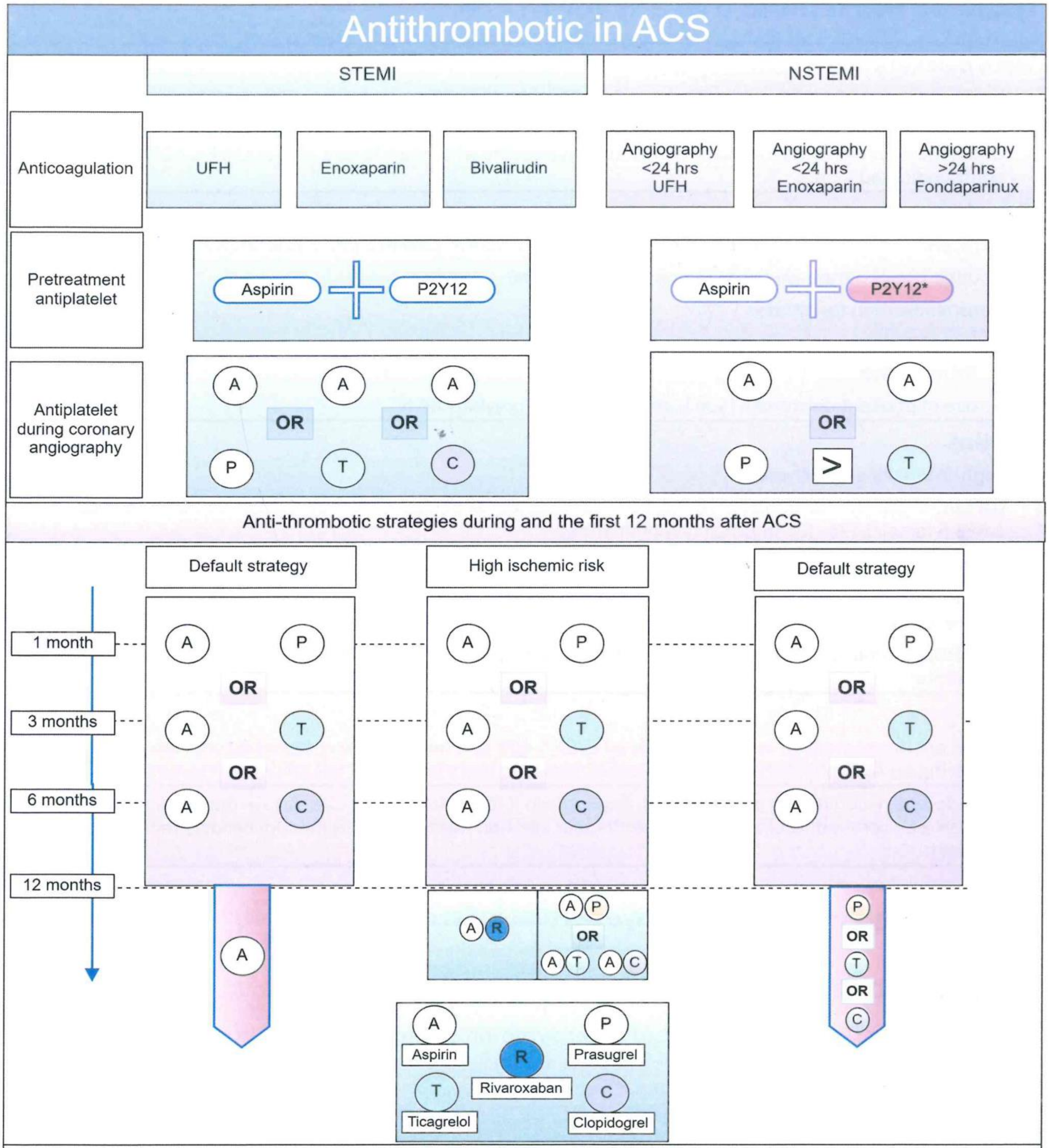
Ibanez B, James S, Agewall S, A. et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39:119-177

PCI:Percutaneous Coronary Intervention; STEMI: ST-segment elevation myocardial infarction

Figure 48-4: Periprocedural antithrombotics in patients with STEMI

STEMI medical therapy

- Long-term antithrombotic therapy is described in Figure 48-5
- Medical therapy for STEMI is described in Table 48-4


Antithrombotic in ACS
STEMI
NSTEMI
Anticoagulation
UFH
Enoxaparin
Bivalirudin
Angiography <24 hrs UFH
Angiography <24 hrs Enoxaparin
Angiography >24 hrs Fondaparinux
Pretreatment antiplatelet
Aspirin
P2Y12
Aspirin
P2Y12*
Antiplatelet during coronary angiography
A
P
OR
A
T
OR
A
C
A
P
OR
>
A
T
Anti-thrombotic strategies during and the first 12 months after ACS
Default strategy
High ischemic risk
Default strategy
1 month
3 months
6 months
12 months
A
P
OR
A
T
OR
A
C
A
R
A
P
OR
A
T
A
C
P
OR
T
OR
C
A
Aspirin
P
Prasugrel
R
Rivaroxaban
T
Ticagrelol
C
Clopidogrel

Byrne RA, Rossello X, Coughlan JJ, et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J Acute Cardiovasc Care. 2023 Sep 22:zuad107.

STEMI: ST-segment elevation myocardial infarction , NSTEMI: non-ST-elevation myocardial infarction, ACS: acute coronary syndrome, UFH, unfractionated heparin

* Routine pre-treatment with a P2Y 12 receptor inhibitor in NSTE-ACS patients in whom coronary anatomy is not known and early invasive management (<24 h) is planned is not recommended, but pre-treatment with a P2Y 12 receptor inhibitor may be considered in NSTE-ACS patients who are not expected to undergo an early invasive strategy (<24 h) and do not have HBR

Figure 48-5: Long-term antithrombotic regimen post PCI

Table 48-4:Medical therapy for STEMI

Beta blockers

- Intravenous beta-blockers should be considered at the time of presentation in patients undergoing primary PCI without contraindications, with no signs of acute heart failure, and with an SBP >120 mmHg.
- Oral treatment with beta-blockers is indicated in patients with heart failure and/or LVEF ≤ 40% unless contraindicated

Nitrates

- Intravenous nitrates may be useful during the acute phase in patients with hypertension or heart failure
- Routine use of nitrate was not recommended in STEMI
- Contraindication for nitrates
  - » Hypotension
  - » RV infarction
  - » use of phosphodiesterase type 5 inhibitors in the previous 48 h

Statins

- High-intensity statin therapy
- An LDL-C goal of < 1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 1.8–5.5 mmol/L (70–155 mg/dL) is recommended.

ACE/ARB inhibitors

- ACE inhibitors are recommended, starting within the first 24 h of STEMI in patients with evidence of heart failure, LV systolic dysfunction, diabetes, or an anterior infarct.
- An ARB, preferably valsartan, is an alternative to ACE inhibitors in patients who are intolerant of ACE inhibitors

MRA

- MRAs are recommended in patients with an LVEF ≤ 40% and heart failure or diabetes, who are already receiving an ACE inhibitor and a beta-blocker, provided there is no renal failure or hyperkalemia

ACE:angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; LDL-C: low-density lipoprotein cholesterol; LV :left ventricular; LVEF:left ventricular ejection fraction; MRA:mineralocorticoid receptor antagonist;

Non-ST-segment elevation myocardial infarction (NSTEMI)

Diagnostic Criteria

- Persistent chest discomfort or other symptoms suggestive of ischemia + ECG criteria of NSTEMI + troponin level

Chest Pain

- Symptoms of MI: central crushing chest pain, usually severe, persisting for 15 minutes or more. Often accompanied by sweating; nausea, belching or vomiting.

ECG Criteria of NSTEMI Diagnosis

- ST-depression ≥ 0.5 mm in 2 contagious lead and/or T wave inversion ≥ 1 mm in 2 contagious lead
- Normal or non-specific ECG changes

Troponin

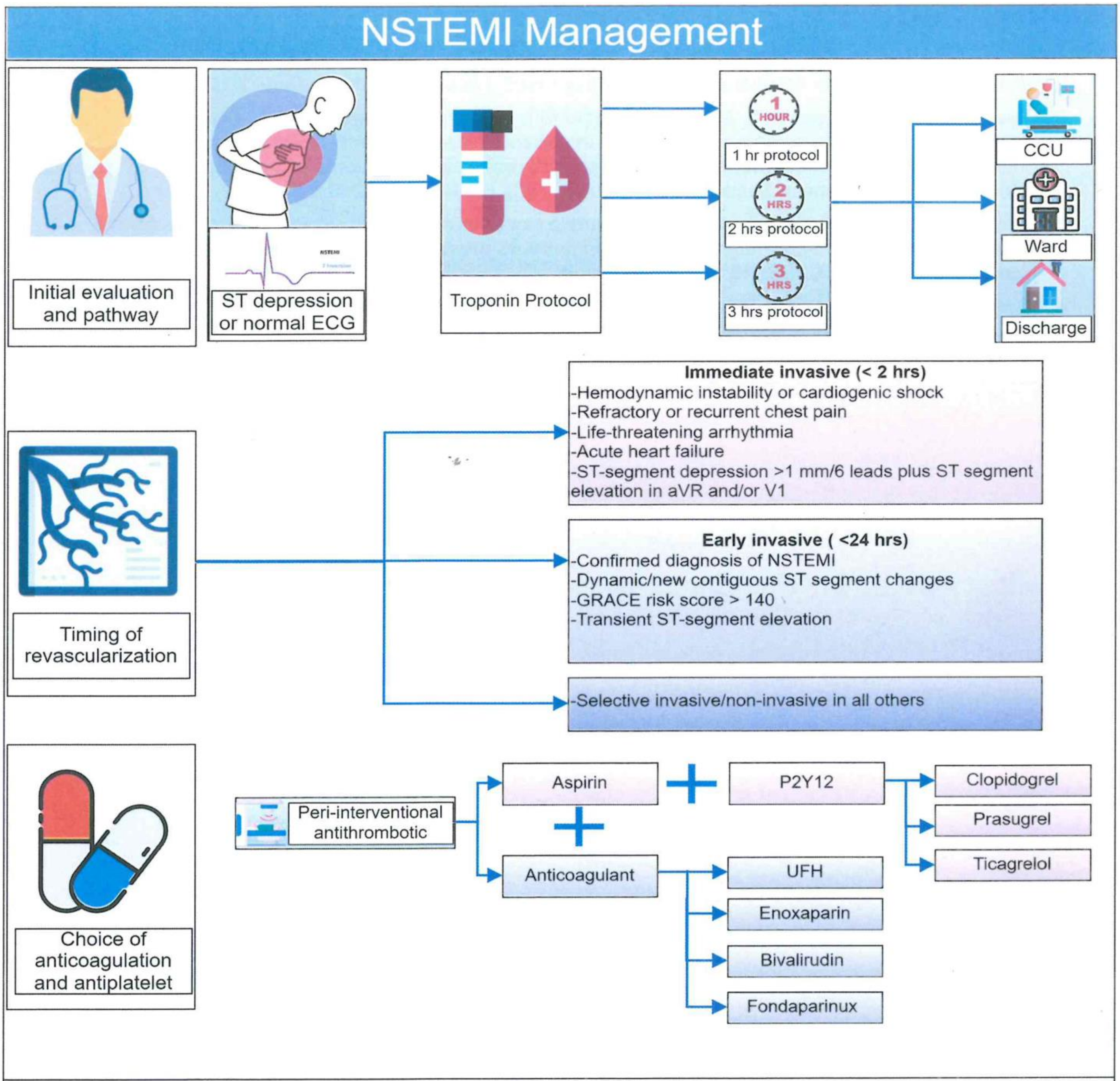
- New guideline from European Society of Cardiology recommended rapid rule out and rule in algorithm using high sensitive troponin.
- Two rapid algorithms: 0/1 hr and 0/2 hrs
- Used in conjunction with clinical and ECG findings, the 0 h/1 h and 0 h/2 h algorithm will allow the identification of appropriate candidates for either hospitalization and early coronary angiography or discharge and outpatient management.
- These algorithms should always be integrated with a detailed clinical assessment and 12-lead ECG, and repeat blood sampling is mandatory in case of ongoing or recurrent chest pain.
- The optimal threshold for 0 hr and change of troponin to rule out and rule in NSTEMI is described in Figure 48 -6

NSTEMI clinical pathway

- Timing of invasive coronary angiography can be categorized into
  - » Immediate invasive in < 2 hours in very high-risk patients
  - » Early invasive in < 24 hours and it is recommended in high-risk patients
  - » Selective invasive in low-risk patients
- NSTEMI clinical pathway including timing of invasive strategy and periprocedural antithrombotics are described in Figure 48-7

NSTEMI medical therapy

- Long-term antithrombotic therapy is described in Figure 48-5
- Medical therapy for NSTEMI is similar to STEMI and it is described in Table 48-4



NSTEMI Management

Initial evaluation and pathway

ST depression or normal ECG

Troponin Protocol

- 1 hr protocol
- 2 hrs protocol
- 3 hrs protocol

- CCU
- Ward
- Discharge

Timing of revascularization

Immediate invasive (< 2 hrs)
-Hemodynamic instability or cardiogenic shock
-Refractory or recurrent chest pain
-Life-threatening arrhythmia
-Acute heart failure
-ST-segment depression >1 mm/6 leads plus ST segment elevation in aVR and/or V1

Early invasive (<24 hrs)
-Confirmed diagnosis of NSTEMI
-Dynamic/new contiguous ST segment changes
-GRACE risk score > 140
-Transient ST-segment elevation

-Selective invasive/non-invasive in all others

Choice of anticoagulation and antiplatelet

Peri-interventional antithrombotic

Aspirin + P2Y12
- Clopidogrel
- Prasugrel
- Ticagrelol

+ Anticoagulant
- UFH
- Enoxaparin
- Bivalirudin
- Fondaparinux

Byrne RA, Rossello X, Coughlan JJ, et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J Acute Cardiovasc Care. 2023 Sep 22:zuad107

CCU: coronary care unit; UFH: unfractionated heparin

Figure 48-7: NSTEMI clinical pathway

References

1. Byrne RA, Rossello X, Coughlan JJ, et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J Acute Cardiovasc Care. 2023 Sep 22:zuad107
2. Ibanez B, James S, Agewall S, A. et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39:119-177
3. Collet JP, Thiele H, Barbato E, et al; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42:1289-1367
4. Angiolillo DJ, Galli M, Collet JP, Kastrati A, O'Donoghue ML. Antiplatelet therapy after percutaneous coronary intervention. Eurointervention. 2022;17:e1371-e1396.

Chapter 49

Hypertensive emergencies

Definitions

- Hypertensive emergencies (HE] are defined as situations where a severely elevated blood pressure (BP), usually a systolic value higher than 180 mmHg and/or a diastolic value higher than 120 mmHg, AND associated with acute, life-threatening organ damage in any of the following key organs:
  - » Brain, arteries, retina, kidney, and/or heart.
- Elevated blood pressure without organ damage is called uncontrolled hypertension or hypertensive urgency

Diagnosis

- All patients with suspected HE will be evaluated through following investigations
  - » CBC
  - » Na, K, urea, and creatinine
  - » LDH
  - » ECG
  - » Fundoscopy
- Further specific investigations should be based on symptoms and aligned with each associated condition's differential diagnosis.
- Diagnosis of HE is presented in Figure 49-1

Management

Hypertensive urgency

- No need for reduction of blood pressure and mainstay of management is life style modification and management of oral pharmacological therapy

Hypertensive emergency

Target blood pressure

- General principle is gradual reduction of blood pressure in a controlled manner
  - » 1st hour: Blood pressure reduction by 25%
  - » 4-6 hours: Blood pressure <160/100 mmHg
  - » 24-48 hours: Blood pressure <140/90 mmHg
- Immediate blood pressure reduction may be needed in some conditions such as acute coronary syndrome, cardiogenic pulmonary edema, aortic dissection.

of neurological HE, in which treatment with dihydropyridine agents such as nicardipine, clevidipine, and a/p blocker (labetalol) are recommended

- Pharmacological therapies for HE is presented in Table 49-1

Disease specific management

- Specific target of blood pressure and the recommended pharmacological therapy for each disease is presented in Figure 49-1

Table 49-1: Intravenous antihypertensive drugs for the management of hypertensive emergencies

Drug	Dose	Site of action	Side effects	Contraindications
Esmolol	500 to 1000 pg/kg i.v. bolus in 1 min or 50-250 ljg/kg/min continuous i.v. infusion	61-blocker	Hypotension, Dizziness, Peripheral ischemia, Infusion site reaction, Bradycardia	Sinus bradycardia, Sick sinus syndrome, Second- or third-degree heart block, Heart failure
Labetalol	0.25-0.5 mg/kg i.v. bolus or 2-4 mg/min i.v. infusion, thereafter 5-20 mg/h	Non-selective ai&G blocker	Symptomatic postural hypotension, Flushing, Acute left ventricular failure	Asthma, Heart failure, Second- or third-degree heart block, Cardiogenic Shock,
Nicardipine	5 mg/h continuous i.v. infusion, increase dose by 2.5 mg/h every 15 min to a maximum dose of 15 mg/h	Ca-channel blocker (arterial dilator)	Dizziness, Flushing, Reflex tachycardia,	Liver failure
Clevidipine	1-2 mg/h i.v. infusion, increase every 2 min with 2 mg/h i.v. bolus or 15-30 mg/min continuous i.v. infusion	Ca-channel blocker (arterial dilator)	Systemic hypotension, Reflex tachycardia	Allergies to soybeans, soy products, eggs or egg products, Defective lipid metabolism, Severe aortic stenosis
Nitroglycerine	5-200 pg/min continuous i.v. infusion, increase by 5 pg/min every 5 min	Nitric oxide donor (venous dilator)	Headache, Reflex tachycardia, Vomiting, Flushing, Methemoglobinemia,	Severe anemia, Right-sided myocardial infarction, Concurrent use with PDE-5 inhibitors
Nitroprusside	0.25-10 pg/kg/min continuous i.v. infusion, increase by 0.5 pg/kg/min every 5 min to a maximal dose only for 10 min	Nitric oxide donor (Arterial and venous dilator)	Thiocyanate intoxication, Methemoglobinemia acidosis, Cyanide poisoning	Concurrent use with PDE-5 inhibitors, Vitamin B12 deficiency
Phentolamine	0.5-1 mg/kg i.v. bolus or 50-300 pg/kg/min continuous i.v. infusion	Non-selective a-blocker	Tachyarrhythmias, Orthostatic hypotension, Chest pain	

References

1. Balahura AM, Moroi ȘI, Scafa-Udrişte A, Weiss E, Japie C, Bartoş D, Bådilå E. The Management of Hypertensive Emergencies-Is There a "Magical" Prescription for All? D Clin Med. 2022:11:3138

Chapter 50

Acute and chronic heart failure

Acute heart failure

Definitions

- **Acute heart failure (AHF) is defined by a rapid or gradual onset of symptoms and/or signs of heart failure (HF) leading the patient to seek urgent medical attention with consequent unplanned hospitalization or an emergency department visit**
- **Acute heart failure may present as a clinical deterioration in patients with a previous diagnosis of HF (acute decompensated HF) or 'de novo' in patients without a previous history of HF.**

Clinical profile

- **According to congestion and perfusion status, heart failure can be categorized into 4 categories:**
  - **Wet-warm profile (70%)**
  - **Wet-cold profile (20%)**
  - **Dry-wet profile (9%)**
  - **Dry-cold profile (1%).**
- **Clinical profiles is described in Figure 50-1**
- **Assessment of congestion and hypoperfusion are discussed in Figure 50-1**

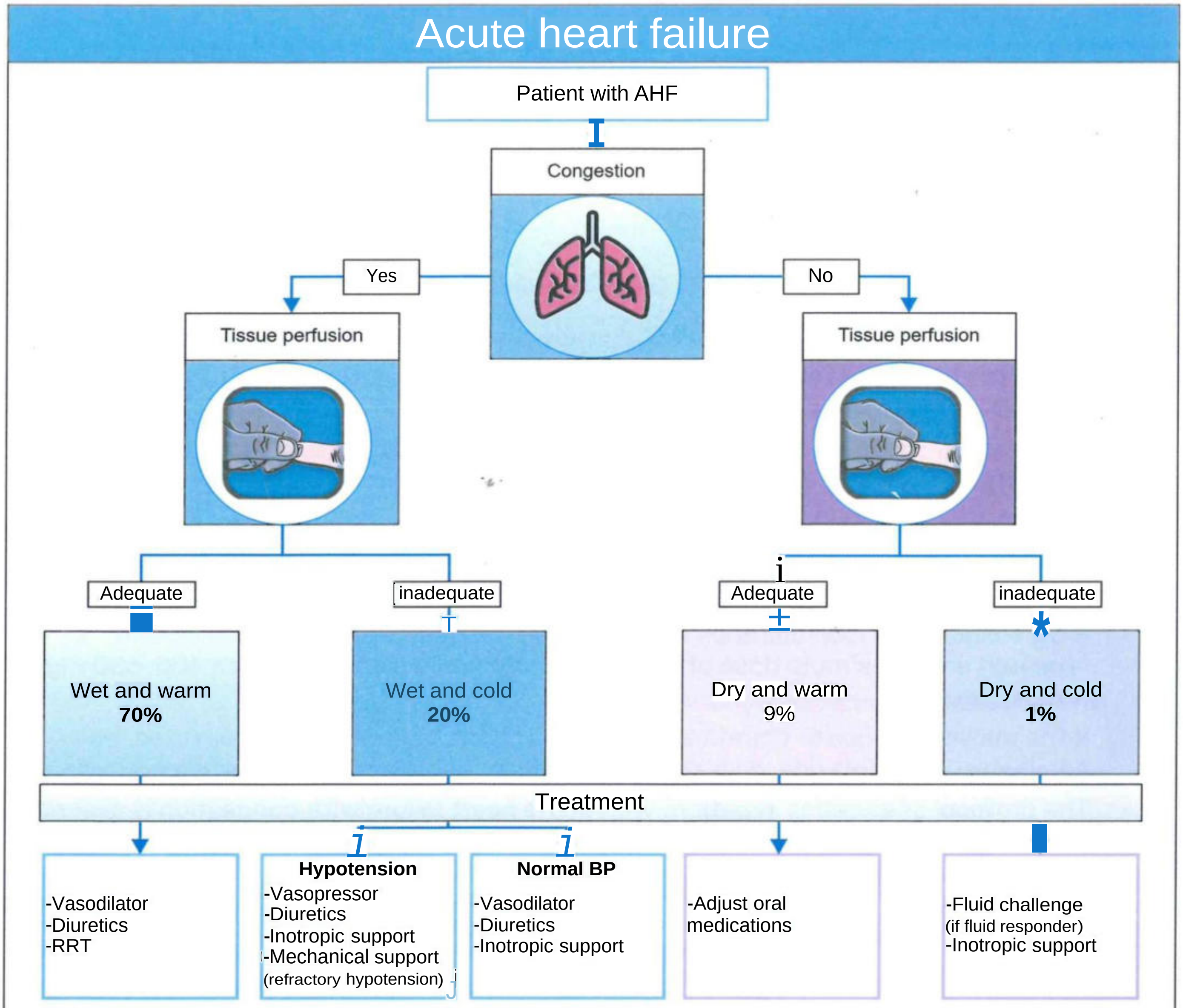
Evaluation and personalized management (7 Ps protocol)

- **Phenotypes**
  - **The assessment of the clinical phenotype based on peripheral perfusion and/or systemic congestions into 4 subtypes**
- **Pathophysiology**
  - **The initial treatment personalized according to leading pathophysiology (for example, vasodilators and/or diuretics to reduce systemic congestion and positive inotropic drugs to improve peripheral perfusion)**
- **Precipitants**
  - **Identification of the precipitants of AHF is essential for providing optimal specific (medical and/or surgical) therapy and for estimating both prognosis and recovery potential.**
- **Pathology**
  - **identification of the underlying cardiac pathology can contribute to tailoring the treatment**
- **Polymorbidities**
  - **The assessment of polymorbidity (for example, renal and hepatic dysfunction) or other relevant conditions (such as pregnancy, bleeding risk and allergies) should be integrated into the management plan.**

- Potential iatrogenic harms associated with diagnostic procedures and treatment should also be considered.
- Patient preferences and ethical considerations
  - » Discussion with the patient or with relatives about resuscitation directives and treatment options are crucial and need to be evaluated early rather than late.
- Medical management of AHF is described in Table 50-1

Table 50-1: Personalized management of AHF according to clinical profiles

Warm-dry	Warm-wet
• Up-titration of disease-modifying oral therapy » Treat comorbidities	• Vasodilators (if fluid redistribution) • Diuretics (if fluid accumulation) • Consider renal replacement therapy
Cold-dry	**Cold-wet**
• Fluid challenge (if fluid-responsive) » Inotropic agent	• Consider vasodilator (if SBP is sufficiently high) • Inotropic agent • Vasopressor (if refractory hypotension) • Diuretics (when perfusion is restored) • Mechanical circulatory support (if shock refractory to drugs)


Acute heart failure
Patient with AHF
Congestion
Yes
No
Tissue perfusion
Tissue perfusion
Adequate
inadequate
Adequate
inadequate
Wet and warm
70%
Wet and cold
20%
Dry and warm
9%
Dry and cold
1%
Treatment
-Vasodilator
-Diuretics
-RRT
Hypotension
-Vasopressor
-Diuretics
-Inotropic support
-Mechanical support
(refractory hypotension)
Normal BP
-Vasodilator
-Diuretics
-Inotropic support
-Adjust oral medications
-Fluid challenge
(if fluid responder)
-Inotropic support

Assessment of congestion and hypoperfusion	**Clinical**	**Echocardiography**	**Hemodynamic**
Congestion	-Bilateral lung crackles -Peripheral edema -Elevated JVP	-Dilated non-collapsed IVC -Bilateral B-lines -High VExUS score	-High CVP > 12 mmHg -High PCWP > 15 mmHg
Low CO (Hypoperfusion)	-Narrow pulse pressure < 25% -Altered mental status -Delayed capillary refill	-Low LVOT VTI	-Increased lactate > 2 mmol/l -Low CPO < 0.6 W -High CO2 gap > 6 mmHg

Marini M, Manfredi K, Battistoni I, et al. Acute heart failure: differential diagnosis and treatment. Eur Heart J Suppl. 2023;[illegible]

AHF: acute heart failure, JVP: jugular venous pressure, IVC: inferior vena cava, CVP: central venous pressure, PCWP: pulmonary capillary wedge pressure, CPO: cardiac power output, LVOT: left ventricular outflow tract, VTI: velocity time integral, CO: cardiac output

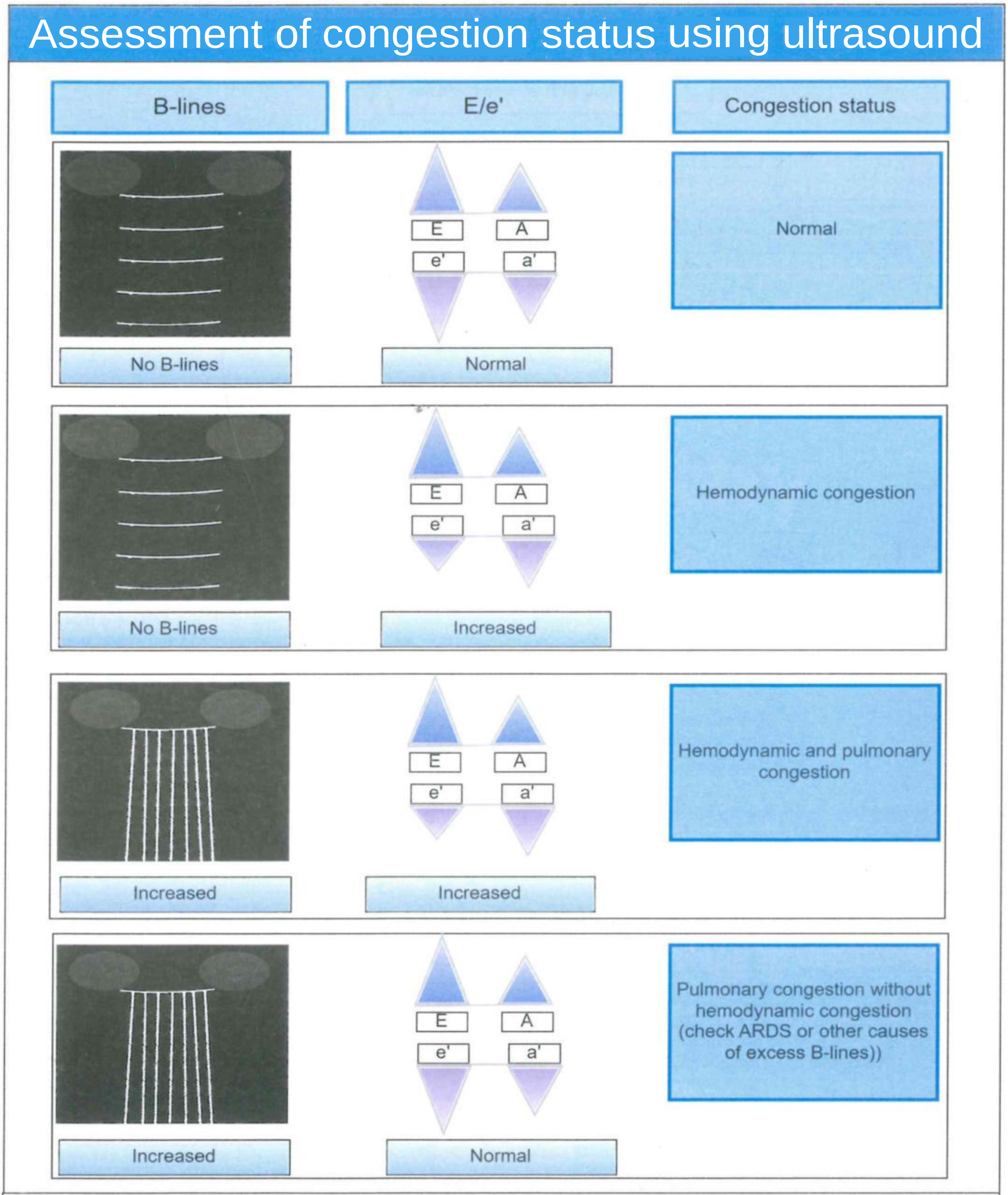
Figure 50-1: Clinical profiles and management of acute heart failure

Assessment of congestion using echocardiography and lung ultrasound

- E/'e is used to assess left ventricular pressure.
- B-lines is used to assess lung water.
- Integration of pulmonary findings and echocardiographic findings are described in Figure 50-2

Approach for diuretic use in acute heart failure with congestion

- Loop diuretics form the backbone of diuretic therapy in acute heart failure,
- In diuretic naive patients with acute heart failure dose of intravenous furosemide is at least 20-40 mg furosemide equivalent.
- In patient with history of oral diuretic therapy at home, diuretic regimen should be 2 times the usual home dose, witlvat least 80 mg/day furosemide equivalents
- Response to loop diuretic is assessed using spot urinary sodium and/or urine volume
  - » Insufficient response is defined as content of < 50-70 mEq/L after 2 h, and/or an hourly urine output < 100-150 mL during the first 6 h
- If the response to loop diuretics is insufficient, the dose should be doubled and repeated until maximum dose of diuretics is attained which is between 400-600 mg of furosemide.
- If the maximum dose of diuretics is reached and the patient is still congested, co-adminstration of thiazide, acetazolamide, and spironolactone migh be helpful
- The protocol of diuretics in patient with acute heart failure with congestion is described in Figure 50-3

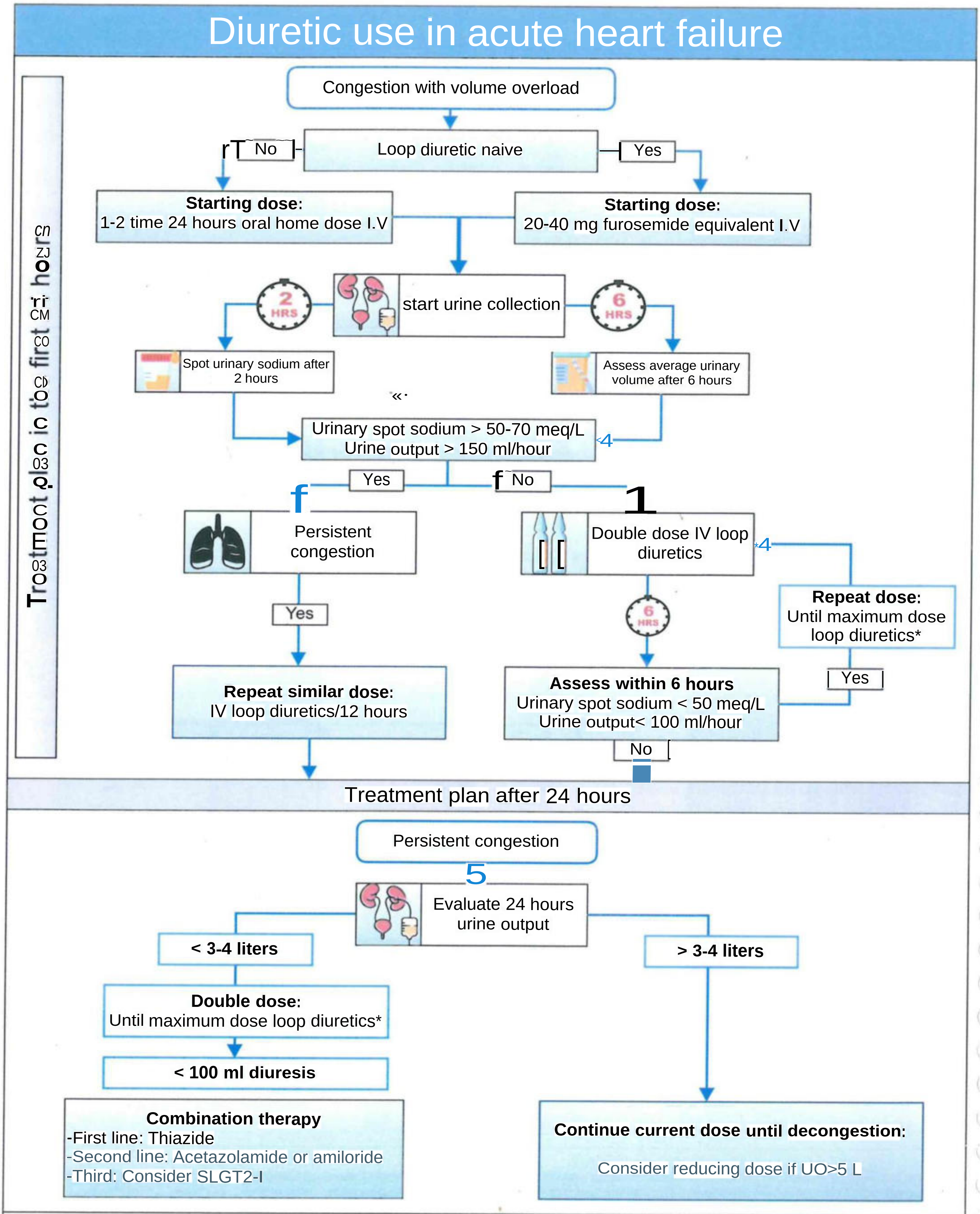


Assessment of congestion status using ultrasound

B-lines	E/e'	Congestion status
No B-lines	Normal	Normal
No B-lines	Increased	Hemodynamic congestion
Increased	Increased	Hemodynamic and pulmonary congestion
Increased	Normal	Pulmonary congestion without hemodynamic congestion (check ARDS or other causes of excess B-lines))

Gargani L, Girerd N, Platz E, et al. Lung ultrasound in acute and chronic heart failure. A Clinical Consensus Statement of the European Association of Cardiovascular Imaging (EACVI). Eur Heart J Cardiovasc Imaging. 2023; 14:jead169.

Figure 50-2: Integrating echocardiography and lung ultrasound to assess congestion status


Diuretic use in acute heart failure
Treatment plan in the first 24 hours
Congestion with volume overload
Loop diuretic naive
No
Yes
Starting dose: 1-2 time 24 hours oral home dose I.V
Starting dose: 20-40 mg furosemide equivalent I.V
2 HRS
start urine collection
6 HRS
Spot urinary sodium after 2 hours
Assess average urinary volume after 6 hours
Urinary spot sodium > 50-70 meq/L
Urine output > 150 ml/hour
Yes
No
Persistent congestion
Double dose IV loop diuretics
Yes
6 HRS
Repeat dose: Until maximum dose loop diuretics*
Yes
Repeat similar dose: IV loop diuretics/12 hours
Assess within 6 hours
Urinary spot sodium < 50 meq/L
Urine output< 100 ml/hour
No
Treatment plan after 24 hours
Persistent congestion
Evaluate 24 hours urine output
< 3-4 liters
> 3-4 liters
Double dose: Until maximum dose loop diuretics*
< 100 ml diuresis
Combination therapy
-First line: Thiazide
-Second line: Acetazolamide or amiloride
-Third: Consider SLGT2-I
Continue current dose until decongestion:
Consider reducing dose if UO>5 L

Mullens W, Damman K, Harjola VP, et al. The use of diuretics in heart failure with congestion - a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2019;21:137-155.
"The maximal dose for IV loop diuretics is generally considered furosemide 400–600 mg or 10–15 mg bumetanide.
IV: Intravenous, UO: urine output, SLGT2-I: sodium–glucose linked transporter 2 inhibitor

Figure 50-3: Diuretic protocol in acute heart failure with congestion

Pharmacological therapy of loop diuretics

- The pharmacokinetic of common loop diuretic is described in Table 50-2
- Diuretic infusion using stepped protocol as described in Table 50-3

Table 50-2: Pharmacokinetics of common loop diuretics

	Furosemide	Bumetanide	Torsemide
Relative IV potency	40	**1**	20
Initial PO dose	20-40	0.5-1	5-10
Maintenance PO dose	40-240	1-5	**10-20**
Maximum daily IV dose	600	**10**	200
Onset (min)			
Oral	30-60	30-60	30-60
IV	5	2-3	**10**
Metabolism	50% renal	50% hepatic	80% hepatic
Average duration of effect, h	6-8	4-6	6-8

Table 50-3: Stepped diuretic protocol

Step	Furosemid dose	Furosemide dose (IV)	Metolazone
1	≤80 mg	40 mg + 5 mg/hr	**0**
2	81-160 mg	80 mg + 10 mg/hr	5 mg OD
3	161-240 mg	80 mg + 20 mg/hr	5 mg BID
4	> 240 mg	80 mg + 30 mg/hr	5 mg BID
The patient is moved to a higher diuretic dose if urine output is <3 l/day on the current dose			

Chronic heart failure

Definition:

- Clinical syndrome with symptoms and/or signs caused by structural and/or functional abnormality and associated with elevated natriuretic peptide level and/or objective evidence of pulmonary or systemic congestion

Classification

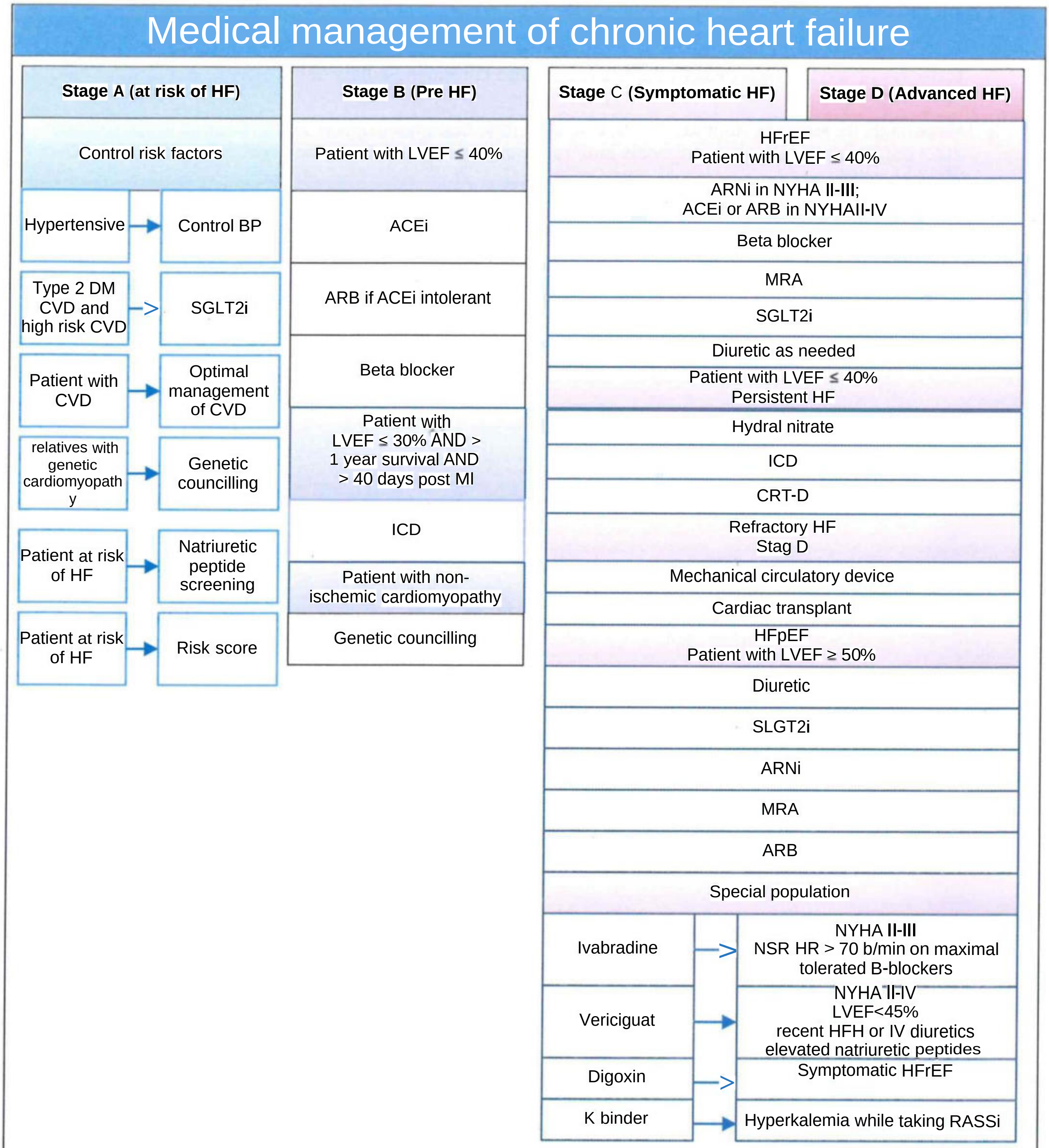
- HF with reduced ejection fraction (HFrEF) – symptomatic HF with LVEF ≤40%
- HF with mildly reduced ejection fraction (HFmrEF) – symptomatic HF with LVEF 41-49% (previously labeled as HF with mid-range ejection fraction)
- HF with preserved ejection fraction (HFpEF) – symptomatic HF with LVEF ≥50%

Stages of heart failure

- **Stage A: At Risk for HF: At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (eg, patients with hypertension, atherosclerotic CVD, diabetes)**
- **Stage B: Pre-HF: No symptoms or signs of HF and evidence of 1 of the following:**
  - **Structural heart disease**
    - **Reduced left or right ventricular systolic function**
    - **Reduced ejection fraction, reduced strain**
    - **Ventricular hypertrophy**
    - **Chamber enlargement**
    - **Wall motion abnormalities**
    - **Valvular heart disease**
  - **Evidence for increased filling pressures**
    - **By invasive hemodynamic measurements**
    - **By noninvasive imaging suggesting elevated filling pressures (eg, Doppler echocardiography)**
  - **Patients with risk factors and Increased levels of BNPs or Persistently elevated cardiac troponin in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary embolus, or myopericarditis**
- **Stage C: Symptomatic HF: Structural heart disease with current or previous symptoms of HF**
- **Stage D: Advanced HF: Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize medical therapy**

Management of heart failure

- **Management of heart failure is based on AHA guideline 2022 and described in Figure 50-4: Management of chronic heart failure according to its stage Figure 50-4**


Medical management of chronic heart failure
Stage A (at risk of HF)
Control risk factors
Hypertensive
Control BP
Type 2 DM CVD and high risk CVD
SGLT2i
Patient with CVD
Optimal management of CVD
relatives with genetic cardiomyopathy
Genetic councilling
Patient at risk of HF
Natriuretic peptide screening
Patient at risk of HF
Risk score
Stage B (Pre HF)
Patient with LVEF ≤ 40%
ACEi
ARB if ACEi intolerant
Beta blocker
Patient with LVEF ≤ 30% AND > 1 year survival AND > 40 days post MI
ICD
Patient with non-ischemic cardiomyopathy
Genetic councilling
Stage C (Symptomatic HF)
Stage D (Advanced HF)
HFrEF
Patient with LVEF ≤ 40%
ARNi in NYHA II-III;
ACEi or ARB in NYHAII-IV
Beta blocker
MRA
SGLT2i
Diuretic as needed
Patient with LVEF ≤ 40%
Persistent HF
Hydral nitrate
ICD
CRT-D
Refractory HF
Stag D
Mechanical circulatory device
Cardiac transplant
HFpEF
Patient with LVEF ≥ 50%
Diuretic
SLGT2i
ARNi
MRA
ARB
Special population
Ivabradine
NYHA II-III
NSR HR > 70 b/min on maximal tolerated B-blockers
Vericiguat
NYHA II-IV
LVEF<45%
recent HFH or IV diuretics
elevated natriuretic peptides
Digoxin
Symptomatic HFrEF
K binder
Hyperkalemia while taking RASSi

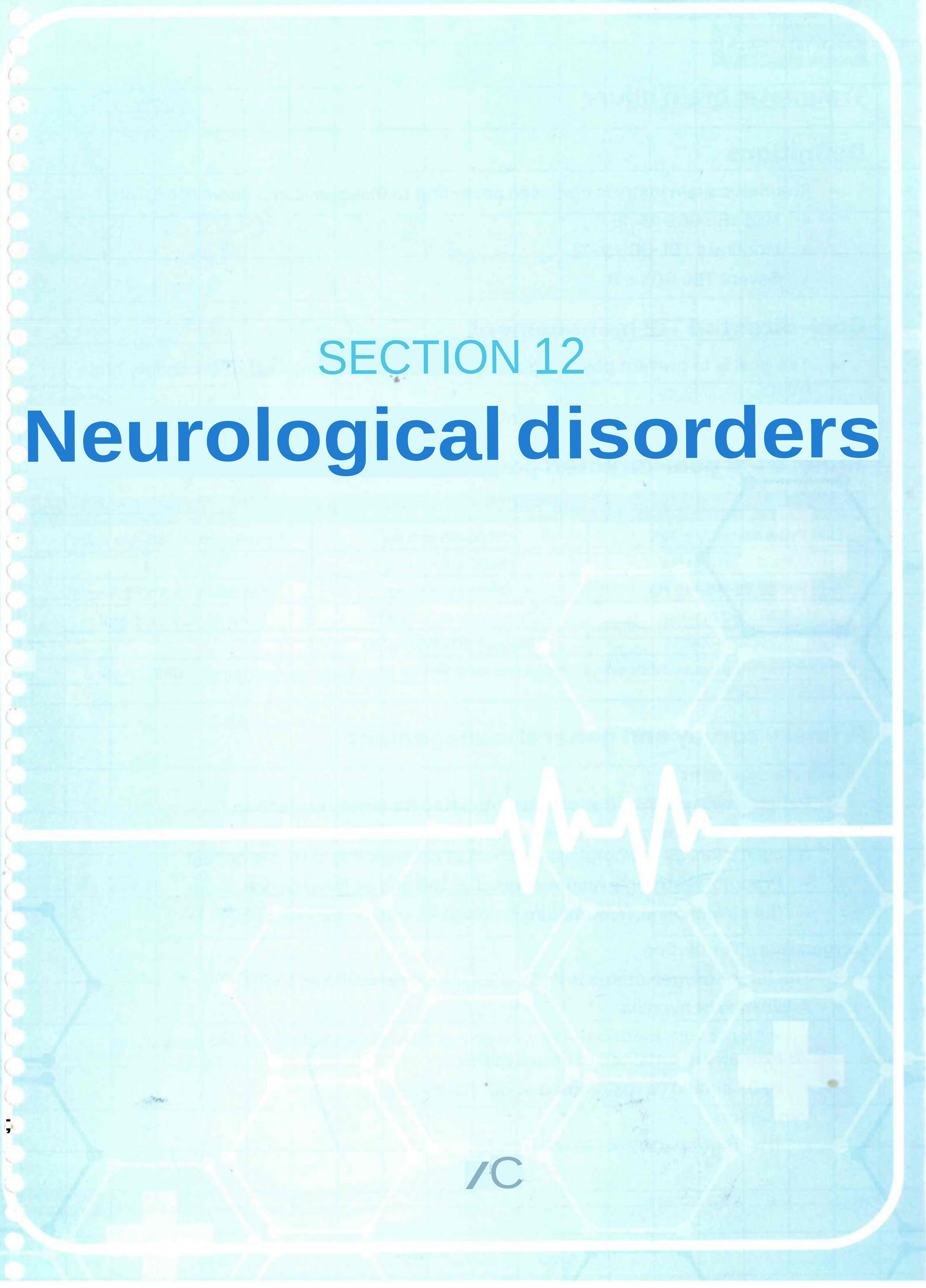
Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145:e895-e1032

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and SGLT2I, sodium glucose cotransporter 2 inhibitor. CRT, cardiac resynchronization therapy; hydral-nitrates, hydralazine and isosorbide dinitrate; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction MRA, mineralocorticoid receptor antagonist; NSR, normal sinus rhythm; NYHA, New York Heart Association, RAASi, renln-angiotensin-aldosterone system inhibitors

Figure 50-4: Management of chronic heart failure according to its stage

References

1. Mullens W, Damman K, Harjola VP, et al. The use of diuretics in heart failure with congestion – a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2019;21:137–155.
2. McDonagh TA, Metra M, Adamo M, et al; ESC Scientific Document Group. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023:ehad195
3. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145:e895–e1032



SECTION 12

Neurological disorders

Chapter 51

Traumatic brain injury

Definitions

- Traumatic brain injury is classified according to Glasgow Coma Score (GCS) into
    - » Mild TBI: GCS 13–15
    - » Moderate TBI: GCS 9–12
    - » Severe TBI: GCS ≤ 8

Goal-directed TBI management

- The goal is to prevent physiological derangement that may lead to secondary brain injury
- The goal directed TBI management is described in Table: 51-1

Table: 51-1: goal-directed parameters TBI

Goal-directed parameters		
Pulse oximetry ≥ 90%	ICP 20–25 mm Hg	Serum sodium 155–145 mEq/L
Pa02 > 60 mm Hg	Pbt02 ≥15 mm Hg	INR ≤1.4
PaC02 35–45 mm Hg	CPP ≥ 60 mm Hg	Platelets ≥ 75 X 10 3 /mm 3
SBP >100 mm Hg	Temperature 36°–38°C	Hemoglobin ≥ 8 g/dL
pH 7.35–7.45	Glucose 80–180 mg/dL	

ICP: intracranial pressure: SBP: systolic blood pressure, Pbt02: brain tissue oxygen tension, CPP: cerebral perfusion pressure

Primary survey and general management

Airway Management

- Patients with a GCS ≤ 8 should be intubated for airway protection
- Sedative and analgesic choices should include short acting agents through the initial resuscitation, as temporal assessment of neurological status is critical
    - » Propofol is strongly recommended as the choice for sedation,
    - » Succinylcholine, Rocuronium bromide – paralytic for induction

Oxygenation/Ventilation

- The target oxygen status is Pa02 ≥ 100 mmHg and 02 Sat ≥ 90%
- Avoidance of hypoxia
    - » Patients with moderate TBI who do not require intubation should have pulse oximetry maintained to at least 90%.
    - » Pa02 should be maintained at 80-120 mmHg
- Ventilation
    - » The target PaC02 is (35-40 mmHg)

  - Hyperventilation should be avoided during the first 24 h after injury when cerebral blood flow (CBF) often is reduced critically.
  - Therapeutic hyperventilation may be necessary for brief periods when there is acute neurological deterioration that coincides with a cerebral herniation syndrome or for refractory elevations in intracranial pressure (ICP)
  - If hyperventilation is used, jugular venous oxygen measurement is recommended to monitor oxygen delivery

Blood Pressure, Volume Resuscitation, Anemia, and Coagulopathy

- Blood Pressure goal
  - Maintaining SBP at ≥ 100 mmHg
  - Normal saline fluid should be used as the initial method of maintaining euvolemia to achieve the target blood pressure.
  - Initiate norepinephrine if cerebral perfusion pressure (CPP) < 60 mmHg despite appropriate volume resuscitation.
- Blood volume goal.
  - Euvolemia should be maintained in TBI management.
  - In many cases a central venous pressure (CVP) monitor will be placed. A CVP goal of 5-7 mmHg correlates with euvolemia but should be assessed in the context of the individual patient's clinical picture. CVP or other types of invasive monitoring are recommended in patients with severe TBI requiring ventriculostomy or intubation.
  - Brain-injured patients should be maintained in a euvolemic state with volume replacement of blood products and crystalloid.
  - The initial resuscitation fluid should be normal saline. Hypertonic saline should only be used as a secondary osmotic agent in ICP control.
  - Volume resuscitation to achieve euvolemia should NOT be withheld to prevent concerns with cerebral edema.
  - Conversely, hypervolemia should be avoided as it is associated with increased incidence of ARDS in TBI patients.
- Anemia - The target is to keep hemoglobin concentration > 8 g/dl.
- Coagulation - coagulation panels should be followed closely.
  - The target INR is ≤ 1.4
  - Fresh frozen plasma (FFP), Vitamin K, Factor VII, should be administered, as clinically indicated, in order to correct coagulopathy.
  - INR and platelet count should be corrected in anticipation of placement of ventriculostomy, or other intracranial surgery.
  - Platelets should be transfused for a platelet count < 75 x 103 / mm^3.

Anti-seizure Prophylaxis

- Post traumatic seizures are a recognised complication of closed head injuries with incidence depending largely on severity of injury.
- Post traumatic seizures (PTS) are classified as either
  - Immediate, early (0-7 days) or
  - Late/delayed (>7 days)

Table 51-2: Berne-Norwood criteria

Risk category	Criteria
Low risk	No moderate or high risk criteria
Moderate risk	• Subdural or epidural hematoma > 8cm • Contusion or intraventricular hemorrhage > 2 cm • Multiple contusions per lobe • Evidence of progression on imaging at 24 hrs • Subarachnoid hemorrhage with abnormal CT angiography
High risk	• Evidence of progression on imaging at 72 hours • Craniotomy • ICP monitor placement

Early Tracheostomy

- VISAGE score ≥ 3 predicts weaning success
- Early tracheostomy within 7 days is recommended to reduce mechanical ventilation days and incidence of ventilator associated pneumonia
- VISAGE score is described in Table: 51-3

Table: 51-3:VISAGE score to predict weaning success

Extubation success score	Assigned points
Age < 40	1
Visual pursuit	1
Swallowing attempt	1
Glasgow coma score > 10	1

Electrolytes and glucose goals

- Serum Electrolyte
  - » The baseline goal for electrolytes (such as, sodium) will be to maintain within normal range (Na 135-145 mmol/L)
  - » In the treatment of elevated ICP with hypertonic saline, Na goal increases to a target of 145 mmol/L (lower threshold) and 160 mmol/L (upper threshold).
- Glucose Monitoring
  - » The glucose level should be maintained between 150 and 180 mg/dl.
  - » Serum glucose should be monitored frequently following the initiation of nutritional support, particularly in patients with known or suspected diabetes mellitus.
  - » In the ICU, initial treatment with regular insulin for hyperglycemia is recommended, with subsequent transition to other patient specific regimens per team.

Nutritional Support

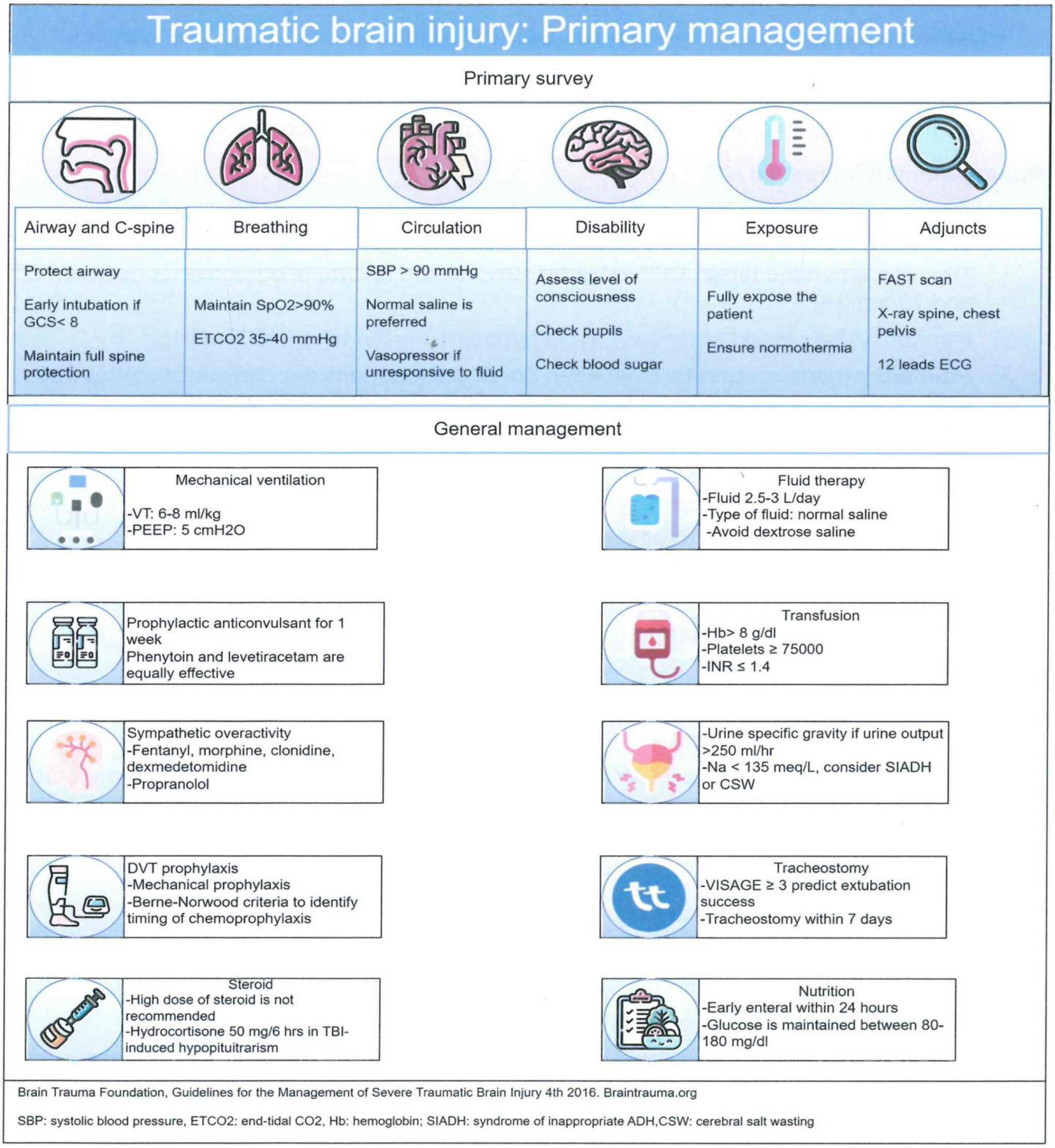
- Nutritional support should be initiated via gastric or enteral route within 24 hours post injury
- Feeding patients to attain basal caloric replacement at least by the fifth day and at most by the seventh day post-injury is recommended to decrease mortality.
- TPN should be utilized cautiously in patients with TBI due to the high glucose concentrations of hyperalimentation solutions.

Non-brain surgery in patients with TBI

- Non-Emergent surgeries that require general anesthesia, such as orthopedic procedures and plastic surgery, should be avoided in BOTH moderate and severe TBI patients until it is clear that the brain injury has stabilized or resolved.
- In the case of emergency surgeries, priority should be given to maintain target physiological parameters such as systolic blood pressure > 100 mmHg (or higher if ICP is elevated), and oxygenation (Pa02 ≥ 100 mmHg and Pulse Ox ≥ 90%) in all patients suspected of having a TBI.

Prevention of paroxysmal sympathetic activity (PSA)

- Non-selective beta blocker propranolol at dose 20 mg/8 hrs. The dose should be increased to 240 mg/day to maintain heart rate below 100 /min.
- Other medications that minimize PSA including clonidine, dexmedetomidine, fentanyl



Traumatic brain injury: Primary management

Primary survey

Airway and C-spine	Breathing	Circulation	Disability	Exposure	Adjuncts
Protect airway Early intubation if GCS< 8 Maintain full spine protection	Maintain SpO2>90% ETCO2 35-40 mmHg	SBP > 90 mmHg Normal saline is preferred Vasopressor if unresponsive to fluid	Assess level of consciousness Check pupils Check blood sugar	Fully expose the patient Ensure normothermia	FAST scan X-ray spine, chest pelvis 12 leads ECG

General management

Mechanical ventilation
-VT: 6-8 ml/kg
-PEEP: 5 cmH2O

Fluid therapy
-Fluid 2.5-3 L/day
-Type of fluid: normal saline
-Avoid dextrose saline

Prophylactic anticonvulsant for 1 week
Phenytoin and levetiracetam are equally effective

Transfusion
-Hb> 8 g/dl
-Platelets ≥ 75000
-INR ≤ 1.4

Sympathetic overactivity
-Fentanyl, morphine, clonidine, dexmedetomidine
-Propranolol

-Urine specific gravity if urine output >250 ml/hr
-Na < 135 meq/L, consider SIADH or CSW

DVT prophylaxis
-Mechanical prophylaxis
-Berne-Norwood criteria to identify timing of chemoprophylaxis

Tracheostomy
-VISAGE ≥ 3 predict extubation success
-Tracheostomy within 7 days

Steroid
-High dose of steroid is not recommended
-Hydrocortisone 50 mg/6 hrs in TBI-induced hypopituitrarism

Nutrition
-Early enteral within 24 hours
-Glucose is maintained between 80-180 mg/dl

Brain Trauma Foundation, Guidelines for the Management of Severe Traumatic Brain Injury 4th 2016. Braintrauma.org

SBP: systolic blood pressure, ETCO2: end-tidal CO2, Hb: hemoglobin; SIADH: syndrome of inappropriate ADH,CSW: cerebral salt wasting

Figure 51-1: Primary survey and general management of patient with TBI

Management of increased intracranial pressure

Intracranial Pressure (ICP) Monitoring

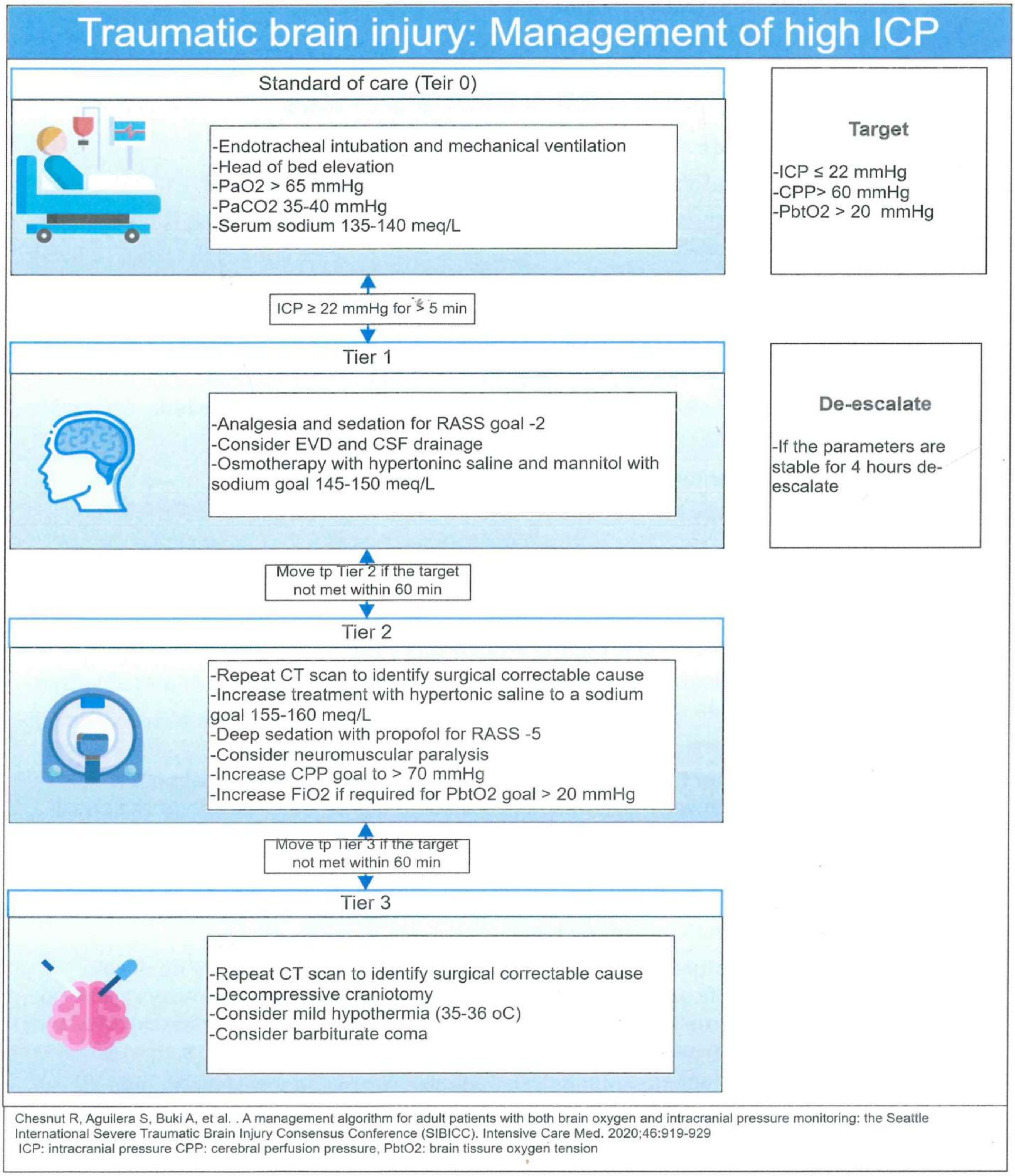
Indications of ICP monitoring

- Salvageable patients with severe TBI (GCS 3-8 after resuscitation) and an abnormal CT scan (hemorrhage, contusions, swelling, herniation or compressed basal cisterns)
- Patients with severe TBI and normal CT scan if two of the following are noted at admission: age > 40 yrs, unilateral or bilateral posturing, systolic BP < 90 mmHg

Management of increased ICP

- Treating ICP ≥ 22 mm Hg is recommended because values above this level are associated with increased mortality.
- The recommended target CPP value for survival and favorable outcomes is between 60 and 70 mm Hg.
- Monitor systolic blood pressures avoid hypotension, Systolic < 100 mmHg.
- Maintain patient temperature between 36-37 Celsius; consider early antipyretics and cooling blankets. Early prophylactic hypothermia IS NOT recommended
- Consider repeat CT: a repeat CT scan of the brain should be considered to rule out the development of a surgical mass or unexpected intracranial lesion
- TIER 0 (Standard of care)
  - » Head of patient's bed to be placed at ≥ 30 degrees.
  - » Sedation and analgesia using recommended agents (propofol, fentanyl) in intubated patients. Pain relief and sedation are appropriate initial modalities for treatment of intracranial hypertension.
  - » Target serum sodium (135-140 meq/L)
- TIER 1
  - » Start Tier if ICP ≥ 22 mmHg
  - » Use of CSF drainage to lower ICP in patients with an initial GCS ≤ 6 during the first 12 h after injury may be considered.
  - » Osmotherapy with hypertonic saline and mannitol with sodium goal 145-150 meq/L
- TIER 2
  - » Start Tier 2 if target goals could not be achieved within 60 min.
  - » Repeat CT scan to identify surgical correctable cause.
  - » Increase treatment with hypertonic saline to a sodium goal 155-160 meq/L
  - » Deep sedation with fentanyl 25-150 mcg/hr IV infusion
  - » Propofol 10-50 mcg/kg/hr IV infusion for Richmond Agitation Sedation Score propofol for RASS -5.
  - » Consider neuromuscular paralysis.
  - » Increase CPP goal to > 70 mmHg.
  - » Increase Fi02 if required for Pbt02 goal > 20 mmHg.
- TIER 3
  - » Start Tier 3 if target goals could not be achieved within 60 min.
  - » Repeat CT scan to identify surgical correctable cause

- Decompressive craniotomy
- Consider mild hypothermia (35-36 oC)
- Consider barbiturate coma



Traumatic brain injury: Management of high ICP

Standard of care (Teir 0)

-Endotracheal intubation and mechanical ventilation
-Head of bed elevation
-PaO2 > 65 mmHg
-PaCO2 35-40 mmHg
-Serum sodium 135-140 meq/L

Target

-ICP ≤ 22 mmHg
-CPP> 60 mmHg
-PbtO2 > 20 mmHg

ICP ≥ 22 mmHg for ≥ 5 min

Tier 1

-Analgesia and sedation for RASS goal -2
-Consider EVD and CSF drainage
-Osmotherapy with hypertoninc saline and mannitol with sodium goal 145-150 meq/L

De-escalate

-If the parameters are stable for 4 hours de-escalate

Move tp Tier 2 if the target not met within 60 min

Tier 2

-Repeat CT scan to identify surgical correctable cause
-Increase treatment with hypertonic saline to a sodium goal 155-160 meq/L
-Deep sedation with propofol for RASS -5
-Consider neuromuscular paralysis
-Increase CPP goal to > 70 mmHg
-Increase FiO2 if required for PbtO2 goal > 20 mmHg

Move tp Tier 3 if the target not met within 60 min

Tier 3

-Repeat CT scan to identify surgical correctable cause
-Decompressive craniotomy
-Consider mild hypothermia (35-36 oC)
-Consider barbiturate coma

Chesnut R, Aguilera S, Buki A, et al. . A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med. 2020;46:919-929
ICP: intracranial pressure CPP: cerebral perfusion pressure, PbtO2: brain tissue oxygen tension

Figure 51-2: Management of increased ICP

Surgical management of TBI

Epidural Hematomas

- Epidural hematoma should be surgically evacuated if
  - » epidural hematoma (EDH) of greater than 30 cm3
  - » acute EDH, GCS <9, and anisocoria
- EDH of less than 5 mm midline shift in patients with GCS >8 and no focal neurological deficit can be closely monitored in an ICU with serial CT scans

Acute Subdural Hematomas

- Acute subdural hematomas [SDH) should be evacuated emergently if
  - » (SDH) with a thickness of greater than 10 mm or 5 mm of midline shift on CT scan regardless of the GCS
  - » SDH less than 10 mm thickness and less than 5 mm midline shift should be evacuated emergently if the patient has: GCS decrease by 2 points, asymmetric pupils or fixed pupils, or ICP > 20 mmHg

Subarachnoid Hemorrhage

- All patients with GCS <9 and SAH should have a ventriculostomy inserted.

Parenchymal Lesions

- Intraparenchymal hemorrhage (IPH)should be evacuated if
  - » medically refractory ICP elevations, or significant mass effect
  - » Frontal or temporal contusions with IPH >20 cm3 and >5 mm shift or cistern compression in patients with GCS 6-8
  - » IPH >50 cm3

Diffuse medical-refractory cerebral edema and elevated ICP

- Decompressive craniectomy for refractory elevated ICP (unilateral or bilateral) within 48 hours of injury is an option in TIER 2

Posterior Fossa Mass Lesions

- Patients with posterior fossa (PF) lesions that show distortion, dislocation, or obliteration of the 4th ventricle, or compression or loss of visualization of the basal cisterns, or obstructive hydrocephalus on CT should be evacuated

Depressed Skull Fractures

- Open skull fractures depressed greater than the thickness of the inner and outer table should undergo operative management.
- Open depressed fractures that are less than 1 cm depressed and have no dural penetration, no significant intracranial hematomas, no frontal sinus involvement, no gross cosmetic deformity, no pneumocephalus, and/or no gross wound contamination may be managed non-operatively
- The efficacy of prophylactic antibiotic to minimize the incidence of meningitis in patients with basilar skull fracture is controversial.

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Chapter 52

Acute spinal cord Injury (SCI)

Initial management

Initial assessment

- The initial management of patients with spinal cord injuries (SCI) includes ABCDE

Airway management

- In emergency condition, rapid sequence induction is guided by videolaryngoscope.
- Succinylcholine can be used as early within the first 48 hours after trauma
- In non-emergency condition, use fiberoptic in patient with suspected difficult intubation (mouth opening < 2.5 cm)

Neurological assessment

- The American Spinal Injury Association (ASIA) standard for neurological functional classification is the recommended preferred tool.
- The ASIA score include
  - » Motor score (total = 100 points)
  - » Key muscles : 10 muscles (C5-T1 and L2-S1)
  - » Sensory score (total = 112 points)
  - » Key sensory points : 28 dermatomes

Radiographic Assessment

NEXUS criteria for cervical spine injury (C-spine)

- Imaging is not necessary if age < 60 and all five of the following criteria are fulfilled
  - » Absence of tenderness in the posterior midline
  - » Absence of a neurological deficit
  - » Normal level of alertness (GCS score = 15)
  - » No evidence of intoxication (drugs or alcohol)
  - » No distracting injury/pain

Imaging for C-spine injury

- High-quality computed tomography (CT) imaging of the cervical spine is recommended
- If high-quality CT imaging is not available, a 3-view cervical spine series (anteroposterior, lateral, and odontoid views) is recommended
- Magnetic resonance imaging should be obtained, when feasible, in the first 48 hours after the trauma

Medical management

Hemodynamic management

- Target
  - Hypotension defined as "systolic pressure < 90 mmHg" should be treated
  - Blood pressure augmentation is to maintain mean arterial pressure > 85-90 mmHg for first 7 days (MAP push) if possible with earlier cessation of blood pressure augmentation if no neurological improvement is seen after the first 72 h, or if there is evidence of complete cord transection.
- Tool
  - Volume resuscitation (1-2 liter)
  - Vasopressor (dopamine/norepinephrine)
  - Atropine 0.5 - 1.0 mg for symptomatic bradycardia
  - Avoid phenylephrine in injuries above T6 since the body may not be able to appropriately mount a sympathetic response to bradycardia.

Respiratory complications

- Pulmonary complications following spinal cord injury is common, owing to diaphragm innervation from C3 to C5
- Bundle to facilitate weaning:
  - Abdominal contention belt during periods of spontaneous breathing
  - Active physiotherapy mechanical-assisted insufflation
  - Aerosol therapy combining 62-agonist and anticholinergic
- Tracheostomy
  - Patients with high cervical spine (C2-C5)
  - Patients with lower cervical spine (C6-C7) and after one or more tracheal extubation failure
- Vaccination against influenza and pneumococcus for all patients with respiratory impairment due to spinal cord injury is recommended.

Gastrointestinal Management

- In cases of high-cervical injury, there is impairment in esophageal sphincter control, which may increase rates of gastroesophageal reflux disease (GERD) and lead to delayed gastric emptying with high post-feed residuals
- The incidence of gallbladder disease also increases for patients with SCI above the T10 level as a result of impaired gastric mobility
- In both upper and lower cord injuries, colonic stasis precipitates ileus and there is loss of voluntary control of the external anal sphincter in complete injuries
- Bowel management include:
  - Dietary fluid and fiber intake to increase the water content of their stool to decrease gastric transit time
  - Complete cord injury: contact irritants such as rectal stimulation, suppositories, and enemas to maintain bowel regularity.
- Stress ulcer prophylaxis: proton pump inhibitor 20mg IV/12 hr

Prevention of VTE

- low-molecular weight heparin within 72 h of injury should be initiated, along with intermittent pneumatic compression devices
- Duration of VTE prophylaxis should be at least 8 weeks
- The routine use of IVC filters is not recommended

Urogenital complications

- Increase incidence of urine retention, hydronephrosis, renal stones, and post-renal failure
  - Urinary catheter should be placed in the early course of injury to track fluid balance.
  - Catheter can be removed after initial acute stage and replaced by scheduled intermittent catheterization.
  - Patient who retains some sensation is subjected to void trial.

Pharmacologic Treatment

- Administration of methylprednisolone is highly debated.
- To date, three trials have evaluated the outcomes of the use of corticosteroids in patients with spinal cord injury
- The lack of level one, evidence-based evidence makes the routine use of steroids highly controversial.

Pain management

- Multimodal analgesia including ketamine and opioid during surgical intervention to prevent prolonged pain
- Control neuropathic pain
  - Oral gabapentinoid and tricyclic antidepressant for 6 months

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3. Fehlings MG, Tetreault LA, Wilson et al. A Clinical Practice Guideline for the Management of Acute Spinal Cord Injury: Introduction, Rationale, and Scope. Global Spine 0. 2017;7:84S-94S

SECTION 12

Chapter 53

Acute ischemic stroke and transient ischemic attack

Acute ischemic stroke

- Acute ischemic stroke (AIS) is characterized by the sudden loss of blood circulation to an area of the brain, typically in a vascular territory, resulting in a corresponding loss of neurologic function.
- Consider stroke in any patient presenting with acute neurologic deficit or any alteration in level of consciousness.
- Common stroke signs and symptoms include the following:
  - Abrupt onset of hemiparesis, monoparesis, or (rarely) quadriparesis
  - Hemisensory deficits
  - Monocular or binocular visual loss
  - Visual field deficits
  - Diplopia
  - Dysarthria
  - Facial droop
  - Ataxia
  - Vertigo (rarely in isolation)
  - Nystagmus
  - Aphasia
  - Sudden decrease in level of consciousness
- The central goal of therapy in acute ischemic stroke is to preserve tissue in the ischemic penumbra
- Recanalization strategies, including the administration of intravenous (IV) recombinant tissue-type plasminogen activator (t-PA) and intra-arterial approaches, and many surgical and endovascular techniques.
- Approach for stroke management is described in Figure 53-1

Initial Assessment

ABC (Airway, breathing, circulation)

- Supplemental oxygen to maintain saturation >94% ((hyperoxia may be detrimental in stroke, so no need for high flow oxygen)
- Hyperbaric oxygen is not recommended for patients with AIS except when caused by air embolization.

History and scores

- Determine time of stroke onset
- History: medications, document any atrial fibrillation
  - Type of medications
  - Use of anticoagulants: types and last dose

- Calculate national institute of health stroke scale (NIHSS) and Glasgow coma score (GCS)

Blood pressure management

- Patients who are eligible for treatment with IV alteplase should have their BP lowered so that their BP is <185/110 mm Hg before initiation of therapy and <180/105 mm Hg for the first 24 hours after treatment.
- Agents that are used in lowering blood pressure is described in Table: 53-1

Table: 53-1: Treatment of arterial hypertension in AIS before emergency reperfusion

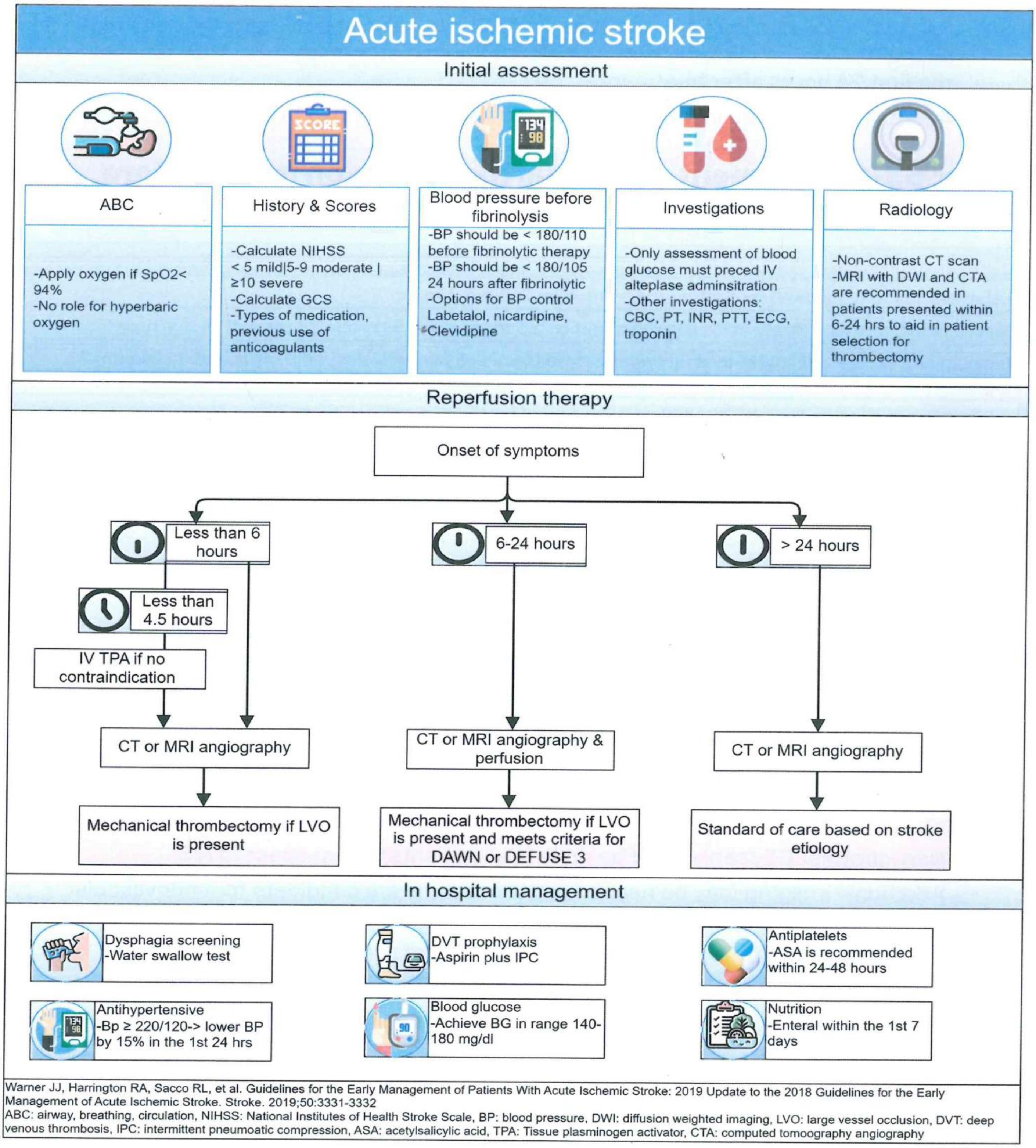
Drug options for acute management of hypertension before thrombolysis
Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h; or
Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h
If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside

Investigations and lab

- Labs: Only the assessment of blood glucose must precede the initiation of IV alteplase in all patients.
- Other investigations SHOULD NOT delay initiation of IV alteplase and may include:
  - » ECG and AF screening
  - » Troponin
  - » CBC
  - » PT/PTT, INR
  - » Creatinine
  - » Beta-HCG for women

Imaging

- Non-contrast CT scan should be done in all patients with suspected AIS
- Additional imaging may be needed in patients who are candidate for endovascular treatment as follow
  - » CT or MRI angiography in patients with onset of symptoms < 6 hours
  - » CT or MRI angiography with perfusion with onset of symptoms 6-24 hours



Acute ischemic stroke

Initial assessment

ABC
-Apply oxygen if SpO2< 94%
-No role for hyperbaric oxygen

History & Scores
-Calculate NIHSS
< 5 mild|5-9 moderate | ≥10 severe
-Calculate GCS
-Types of medication, previous use of anticoagulants

Blood pressure before fibrinolysis
-BP should be < 180/110 before fibrinolytic therapy
-BP should be < 180/105 24 hours after fibrinolytic
-Options for BP control Labetalol, nicardipine, Clevidipine

Investigations
-Only assessment of blood glucose must preced IV alteplase adminsitration
-Other investigations: CBC, PT, INR, PTT, ECG, troponin

Radiology
-Non-contrast CT scan
-MRI with DWI and CTA are recommended in patients presented within 6-24 hrs to aid in patient selection for thrombectomy

Reperfusion therapy

Onset of symptoms

Less than 6 hours
Less than 4.5 hours
IV TPA if no contraindication
CT or MRI angiography
Mechanical thrombectomy if LVO is present

6-24 hours
CT or MRI angiography & perfusion
Mechanical thrombectomy if LVO is present and meets criteria for DAWN or DEFUSE 3

> 24 hours
CT or MRI angiography
Standard of care based on stroke etiology

In hospital management

Dysphagia screening
-Water swallow test

DVT prophylaxis
-Aspirin plus IPC

Antiplatelets
-ASA is recommended within 24-48 hours

Antihypertensive
-Bp ≥ 220/120-> lower BP by 15% in the 1st 24 hrs

Blood glucose
-Achieve BG in range 140-180 mg/dl

Nutrition
-Enteral within the 1st 7 days

Warner JJ, Harrington RA, Sacco RL, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke. Stroke. 2019;50:3331-3332

ABC: airway, breathing, circulation, NIHSS: National Institutes of Health Stroke Scale, BP: blood pressure, DWI: diffusion weighted imaging, LVO: large vessel occlusion, DVT: deep venous thrombosis, IPC: intermittent pneumoatic compression, ASA: acetylsalicylic acid, TPA: Tissue plasminogen activator, CTA: computed tomoography angiography

Figure 53-1: Acute ischemic stroke management protocol

Reperfusion therapy

Intravenous alteplase

- Alteplase administration is described in Figure: 53-2

Inclusion criteria

- Age ≥ 18 years.
- Persistent disabling neurological deficits suggestive of an acute ischemic stroke
- Onset of symptoms between 3 to 4.5 h from last known well or Wake-up and unknown time of onset of symptoms, based on DWI-FLAIR imaging mismatch.

Exclusion criteria

- Significant head trauma or prior stroke in the previous 3 months
- Symptoms suggestive of SAH
- History of previous ICH
- Intraaxial-Intracranial neoplasm
- Recent intracranial or intraspinal surgery within prior 3 months
- Gastrointestinal malignancy or hemorrhage within 21 days
- Known aortic arch dissection or infective endocarditis
- Elevated blood pressure (systolic > 185 mm Hg or diastolic > 110 mm Hg)
- Active internal bleeding in the past 21 days
- Acute bleeding diathesis, including but not limited to:
    - » Platelet count < 100,000/mm3
    - » Therapeutic doses of low molecular weight heparin received within 24 h (e.g., to treat VTE and ACS); this exclusion does not apply to prophylactic doses (e.g., to prevent VTE).
    - » Current use of anticoagulant with INR > 1.7 or PT > 15 s
    - » Current use (i.e., last dose within 48 h in a patient with normal renal function) of a direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect by laboratory tests such as aPTT, INR, TT, or appropriate factor Xa activity assays.
- Blood glucose concentration < 50 mg/dL (2.7 mmol/L) unless corrected prior to administration.
- CT Head demonstrating multilobar infarction or hypodensity involving >1/3 cerebral hemisphere.
- Extensive regions of obvious hypodensity consistent with irreversible injury.

Administration of t-PA

- Drug: Recombinant tissue plasminogen activator (rtPA) or alteplase.
- Weigh the patient; do not estimate body weight.
- Total dose: 0.9 mg/kg t-PA, total dose not to exceed 90 mg.
- Give 10% of the total dose of t-PA by bolus over 1 minutes, then infuse the remaining dose over 1 hour
- After administration of t-PA

  - Avoid indwelling urinary catheter, nasogastric tubes, intra-arterial catheters for 4 hours;
  - Do not give anticoagulant/antiplatelet therapy for 24 hours;
  - Repeat head CT MRI at 24 hours before starting anticoagulant/antiplatelet medications
  - Watch for complications of t-PA, including cerebral hemorrhage and angioedema

Management of complications

Cerebral hemorrhage

- Stop alteplase infusion
- CBC, PT (INR), aPTT, fibrinogen level
- Cryoprecipitate: 10 U infused over 10–30 min administer additional dose for fibrinogen level of <150 mg/dL
- Tranexamic acid 1000 mg IV infused over 10 min OR £-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled
- Hematology and neurosurgery consultations
- Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

Angioedema

- Stop alteplase infusion
- Administer oxygen, monitor saturation
- Monitor airway, check stridor, prepare for possibility of intubation or cricothyrotomy
- Administer IV methylprednisolone 125 mg
- Administer IV diphenhydramine 50 mg
- Administer ranitidine 50 mg IV or famotidine 20 mg IV
- If there is further increase in angioedema, administer epinephrine (0.1%) 0.5 mg intramuscular

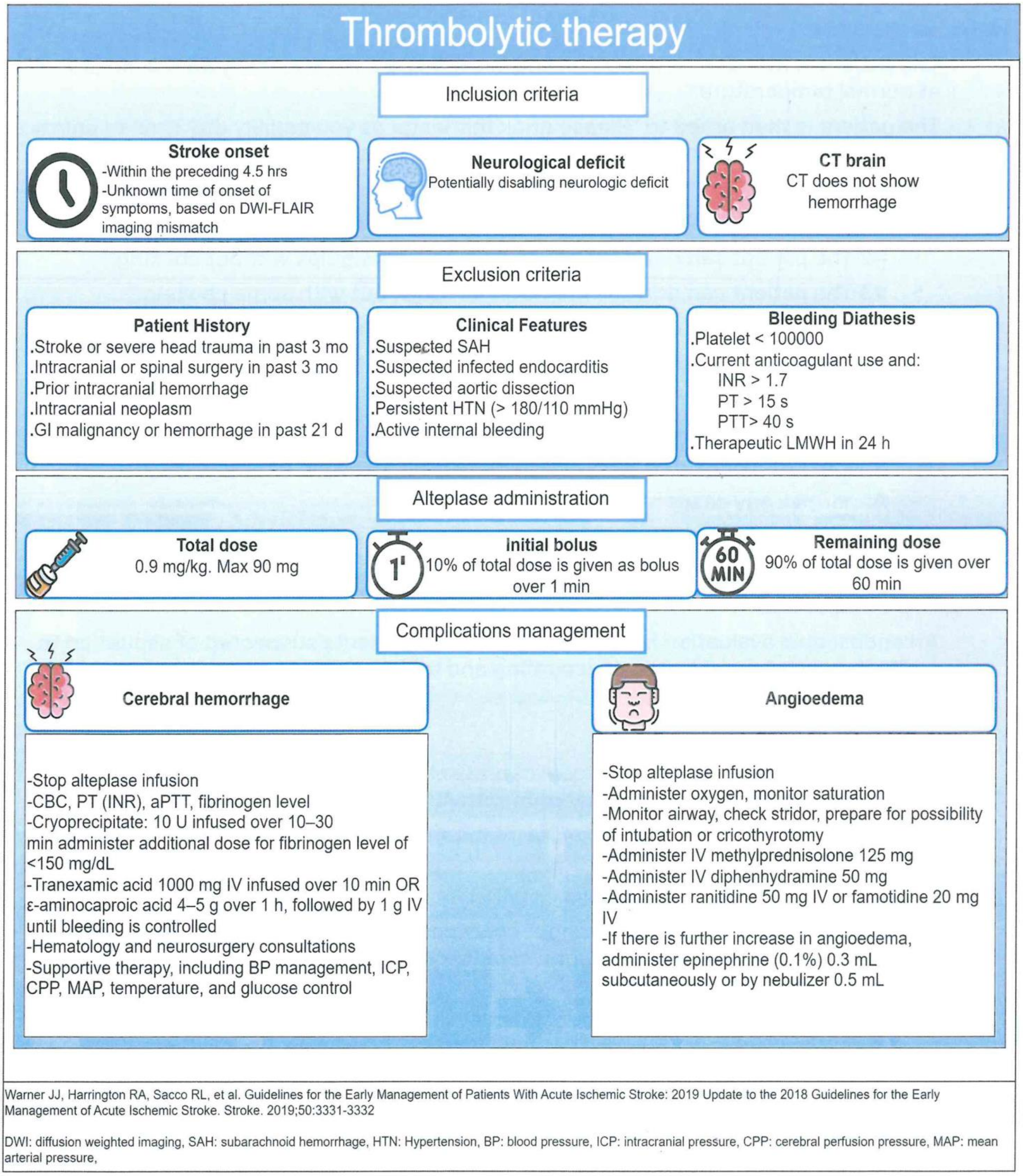
Endovascular management (mechanical thrombectomy)

0-6 hours from symptoms onset

- Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria:
  - prestroke mRS score of 0 to 1;
  - causative occlusion of the internal carotid artery or MCA segment 1 (M1)
  - age ≥18 years;
  - NIHSS score of ≥6 (Level I)
  - ASPECTS of ≥6; (Level I)
  - NIHSS score of <6 (Level Mb)
  - ASPECTS of <6; (Level lib)

6-24 hours from symptoms onset

- Large vessel occlusion in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria



Thrombolytic therapy

Inclusion criteria

Stroke onset
-Within the preceding 4.5 hrs
-Unknown time of onset of symptoms, based on DWI-FLAIR imaging mismatch

Neurological deficit
Potentially disabling neurologic deficit

CT brain
CT does not show hemorrhage

Exclusion criteria

Patient History
.Stroke or severe head trauma in past 3 mo
.Intracranial or spinal surgery in past 3 mo
.Prior intracranial hemorrhage
.Intracranial neoplasm
.GI malignancy or hemorrhage in past 21 d

Clinical Features
.Suspected SAH
.Suspected infected endocarditis
.Suspected aortic dissection
.Persistent HTN (> 180/110 mmHg)
.Active internal bleeding

Bleeding Diathesis
.Platelet < 100000
.Current anticoagulant use and:
  INR > 1.7
  PT > 15 s
  PTT> 40 s
.Therapeutic LMWH in 24 h

Alteplase administration

Total dose
0.9 mg/kg. Max 90 mg

Initial bolus
10% of total dose is given as bolus over 1 min

Remaining dose
90% of total dose is given over 60 min

Complications management

Cerebral hemorrhage

-Stop alteplase infusion
-CBC, PT (INR), aPTT, fibrinogen level
-Cryoprecipitate: 10 U infused over 10–30 min administer additional dose for fibrinogen level of <150 mg/dL
-Tranexamic acid 1000 mg IV infused over 10 min OR ε-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled
-Hematology and neurosurgery consultations
-Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

Angioedema

-Stop alteplase infusion
-Administer oxygen, monitor saturation
-Monitor airway, check stridor, prepare for possibility of intubation or cricothyrotomy
-Administer IV methylprednisolone 125 mg
-Administer IV diphenhydramine 50 mg
-Administer ranitidine 50 mg IV or famotidine 20 mg IV
-If there is further increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL

Warner JJ, Harrington RA, Sacco RL, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke. Stroke. 2019;50:3331-3332

DWI: diffusion weighted imaging, SAH: subarachnoid hemorrhage, HTN: Hypertension, BP: blood pressure, ICP: intracranial pressure, CPP: cerebral perfusion pressure, MAP: mean arterial pressure,

Figure: 53-2: Alteplase administration

In hospital management

Dysphagia screening

Water swallow test

- The patient is asked to sit in a chair, and is handed a cup containing 30-90 mL of water at normal temperature.
- The patient is then asked to "Please drink this water as you usually do." Time to empty a cup is measured, and the drinking profile and episodes are monitored and assessed.
  - Drinking profile
    - #1 The patient can drink all the water in 1 gulp without choking.
    - #2 The patient can drink all the water in 2 or more gulps without choking.
    - #3 The patient can drink all the water in 1 gulp, but with some choking.
    - #4 The patient can drink all the water in 2 or more gulps, but with some choking.
    - #5 The patient often chokes and has difficulty drinking all the water
  - Diagnosis
    - Normal: Completed profile #1 within 5 second
    - Suspected: Completed profile #1 in more than 5 second or profile #2
    - Abnormal: any cases of profiles #3 through 5
  - If the WST is abnormal, patient should be kept NPO and nasogastric tube should be inserted

Endoscopic evaluation

- An endoscopic evaluation is reasonable for those patients suspected of aspiration to verify the presence/absence of aspiration and to determine the physiological reasons for the dysphagia

Anticoagulant

- Urgent anticoagulation, with the goal of preventing early recurrent stroke, is not recommended for treatment of patients with AIS.
- The safety and usefulness of factor Xa inhibitors in the treatment of AIS are not well established.
- Venous thromboembolism prophyaxis (VTE)
  - In immobile stroke patients without contraindications, intermittent pneumatic compression in addition to routine care (aspirin and hydration) is recommended over routine care to reduce the risk of VTE.
  - The benefit of prophylactic-dose subcutaneous heparin (unfractionated or low molecular weight) in immobile patients with AIS is not well established.

Neuroprotective therapy

- No pharmacological or non-pharmacological treatments with putative neuroprotective actions have demonstrated efficacy in improving outcomes after ischemic stroke

Blood pressure management

- In patients with BP ≥220/120 mm Hg who did not receive IV alteplase or mechanical thrombectomy and have no comorbid conditions requiring urgent antihypertensive treatment. It might be reasonable to lower BP by 15% during the first 24 hours after onset of stroke

Lipid-lowering agents

- Statin dose should be maximized to keep LDL-C < 70 mg/dL
- Ezetimibe if LDL-C level ≥ 70 mg/dl despite maximum dose of statins

Glucose

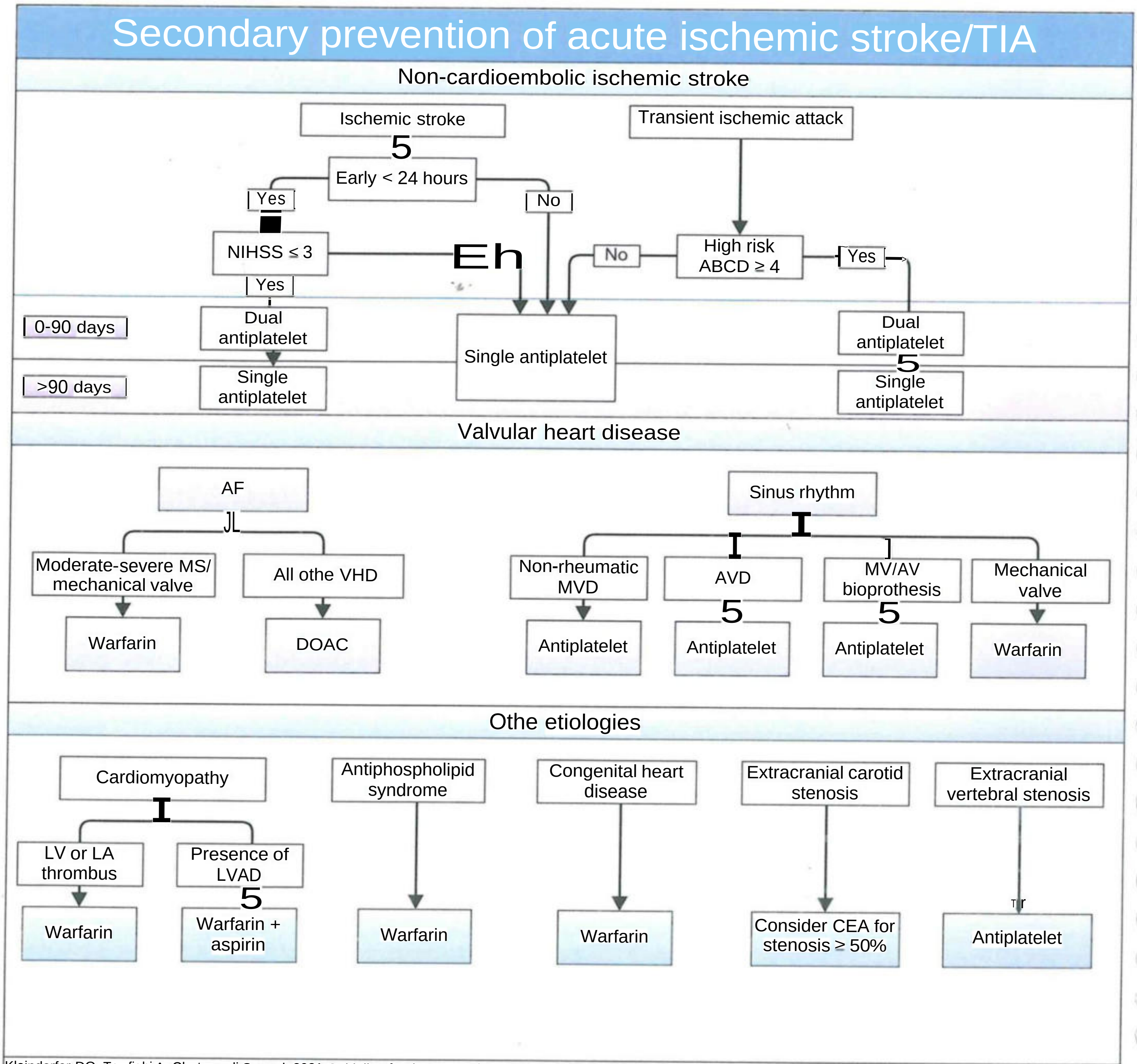
- Blood glucose levels should be maintained in a range of 140 to 180 mg/dL

Nutrition

- Enteral diet should be started within 7 days of admission after an acute stroke.
- For patients with dysphagia, it is reasonable to initially use nasogastric tubes for feeding in the early phase of stroke (starting within the first 7 days) and to place percutaneous gastrostomy tubes in patients with longer anticipated persistent inability to swallow safely (>2–3 weeks).

Secondary prevention of acute ischemic stroke

- Secondary prevention of acute ischemic stroke is described in Figure 53-3


Secondary prevention of acute ischemic stroke/TIA
Non-cardioembolic ischemic stroke
Ischemic stroke
Transient ischemic attack
Early < 24 hours
Yes
No
NIHSS ≤ 3
No
High risk ABCD ≥ 4
Yes
Yes
0-90 days
Dual antiplatelet
Single antiplatelet
Dual antiplatelet
>90 days
Single antiplatelet
Single antiplatelet
Valvular heart disease
AF
Sinus rhythm
Moderate-severe MS/ mechanical valve
All othe VHD
Non-rheumatic MVD
AVD
MV/AV bioprothesis
Mechanical valve
Warfarin
DOAC
Antiplatelet
Antiplatelet
Antiplatelet
Warfarin
Othe etiologies
Cardiomyopathy
Antiphospholipid syndrome
Congenital heart disease
Extracranial carotid stenosis
Extracranial vertebral stenosis
LV or LA thrombus
Presence of LVAD
Warfarin
Warfarin + aspirin
Warfarin
Warfarin
Consider CEA for stenosis ≥ 50%
Antiplatelet

Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52:e364-e467

NIHSS: National Institutes of Health Stroke Scale, DOAC: direct oral anticoagulant, LV: left ventricle, LA: left atrium, LVAD:Left ventricular assisted device, CEA: carotid endartrectomy, VHD: valvular heart disease, MV: mitral valce: AV: aortic valve, AVD: aortic valve disease. MVD: mitral valve disease

Figure: 53-3: Secondary prevention of AIS/TIA

Transient Ischemic Attack (TIA)

Risk stratification and management

- Obtain a 12-lead ECG or review the rhythm strip if available.
- Arrange carotid imaging: ultrasound, CTA or MRA
- $ABCD^2$ score is an ordinal scale that provides risk prediction of stroke after suspected TIA (Table 532)
  - » Low risk: $ABCD^2 < 4$
  - » High risk: $ABCD^2 \geq 4$

Management of TIA

Antiplatelet therapy for non-cardioembolic TIA

- Single antiplatelet for low risk
- Dual antiplatelet for high risk for 90 days then single antiplatelet

Antiplatelet therapy for other patients

- Antiplatelet therapy for secondary prevention is described in

Table: 53-2: $ABCD^2$ risk stratification of TIA

$ABCD^2$ elements	Criteria
Age > 60 years	1
Blood Pressure ≥ 140/90 mmHg on initial evaluation	1
Clinical Features • Speech disturbance without weakness • Unilateral weakness	 1 2
Duration of symptoms • 10 – 59 minutes • 60 minutes or greater	 1 2
Diabetes mellitus in patient's history	1
Total Score	< 4 Low risk ≥ 4 High risk

References

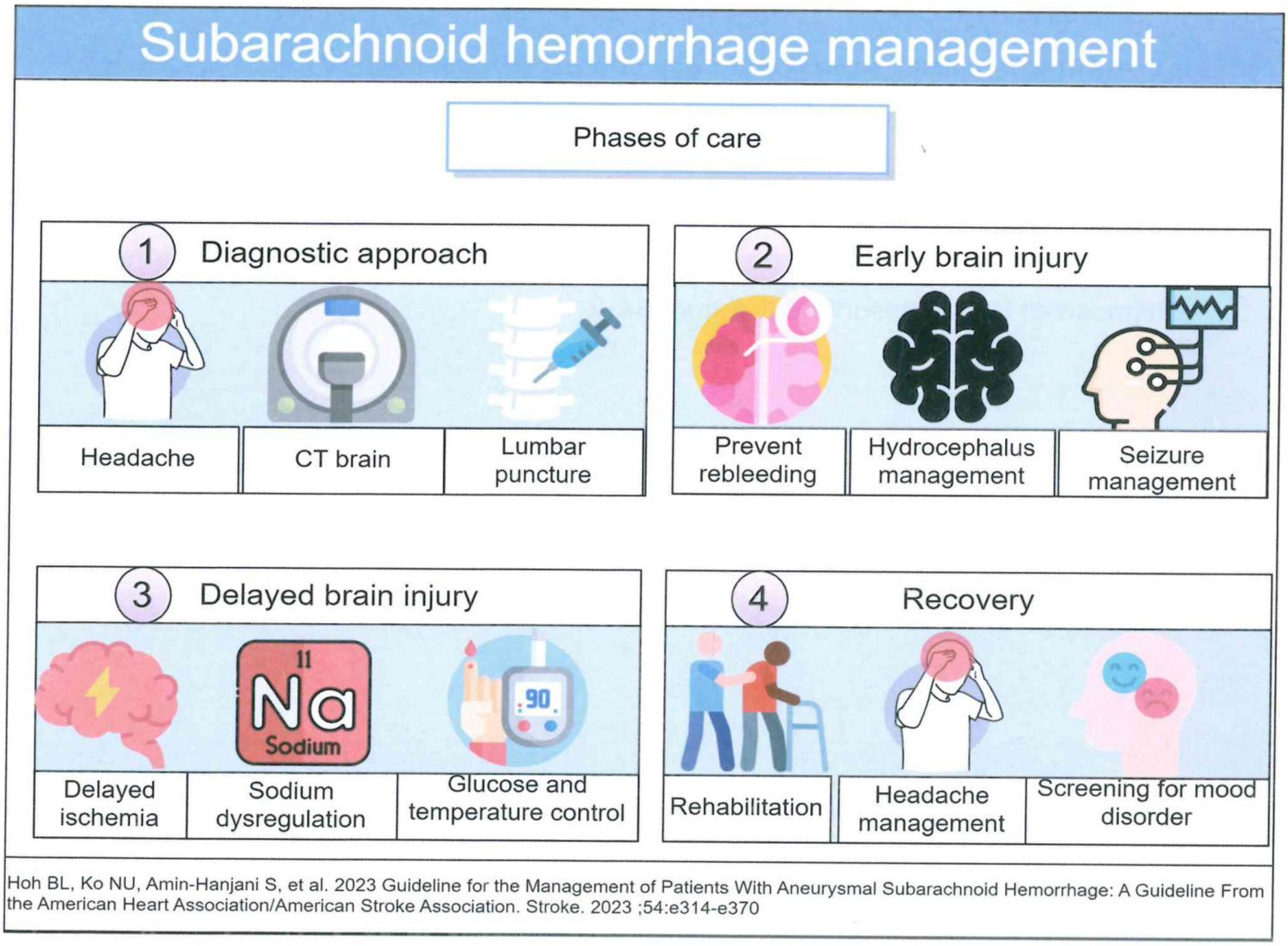
1. Warner OJ, Harrington RA, Sacco RL, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke. Stroke. 2019; 50:3331-3332
2. Patel P, Yavagal D, Khandelwal P. Hyperacute Management of Ischemic Strokes: DACC Focus Seminar. 0 Am Coll Cardiol. 2020; 75:1844-1856
3. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021 0ul;52(7):e364-e467

Chapter 54

Management of Patients with Aneurysmal Subarachnoid Hemorrhage

General Principles

- The overall mortality of SAH is approximately 25 % and significant morbidity amongst the survivors
- The prognosis is related to the amount of blood in the subarachnoid space.
- The most serious complications following the initial bleed are rebleeding and cerebral vasospasm; management of patients with SAH is therefore is largely directed to avoiding these complications
- Phases of care of SAH management are described in Figure 54-1


Subarachnoid hemorrhage management
Phases of care
1 Diagnostic approach
Headache
CT brain
Lumbar puncture
2 Early brain injury
Prevent rebleeding
Hydrocephalus management
Seizure management
3 Delayed brain injury
11
Na
Sodium
90
Delayed ischemia
Sodium dysregulation
Glucose and temperature control
4 Recovery
Rehabilitation
Headache management
Screening for mood disorder

Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2023 ;54:e314-e370

Figure 54-1: phases of care of subarachnoid hemorrhage

Diagnosis of SAH

Clinical presentation

- The hallmark of presentation is unexplained acute severe headache (thunderclap)
  - » Sudden agonising headache peaking in intensity within 1 to 5 minutes.

- Otawa criteria: patient require additional investigation for SAH if they meet any of the following criteria:
  - Thunderclap headache (instantly peaking pain)
  - Age ≥ 40 years
  - Neck pain or stiffness.
  - Witnessed loss of consciousness.
  - Onset during exertion.
  - Limited or painful neck flexion.

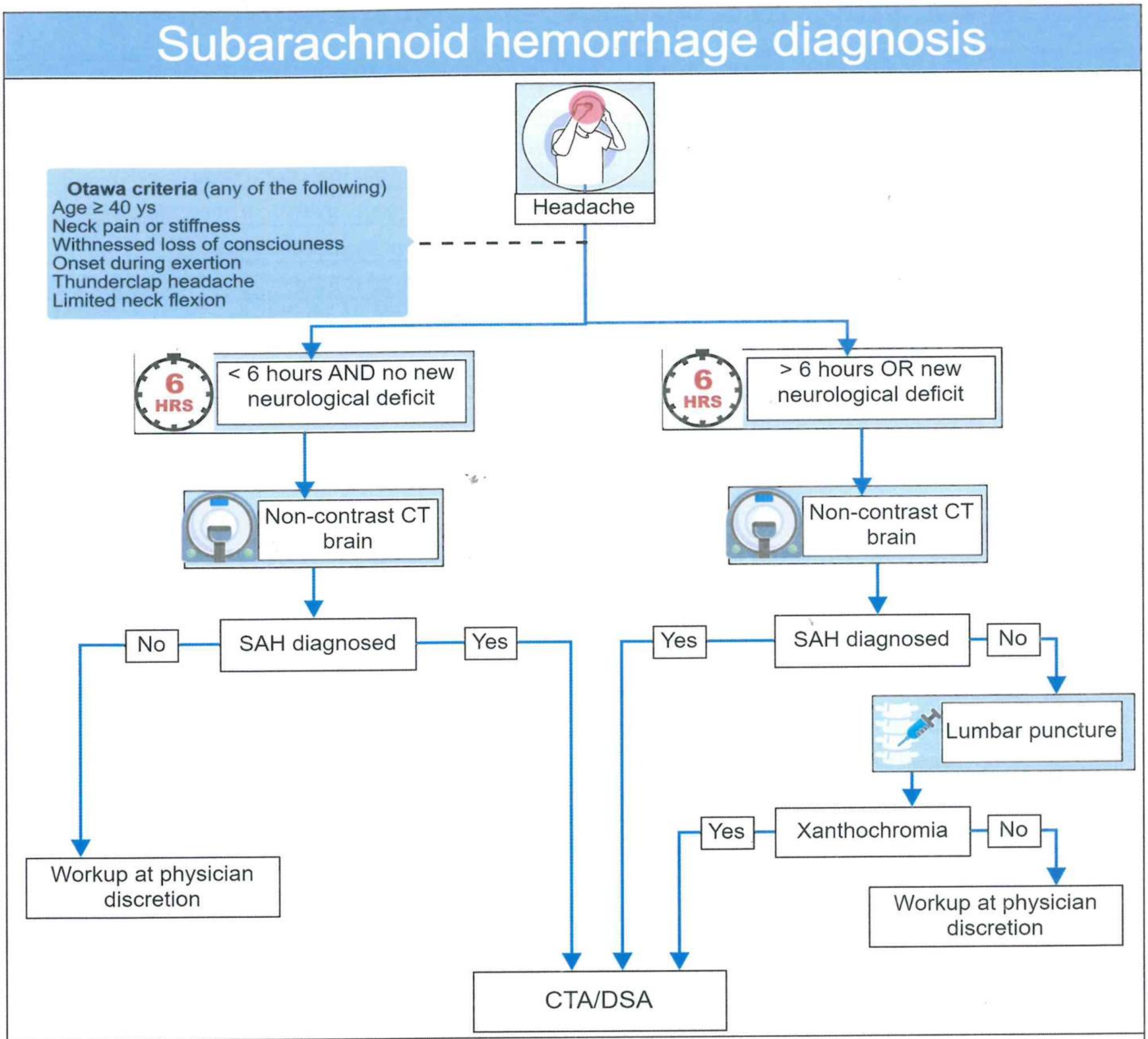
Radiological imaging

Patient presented <6 hours from onset of symptoms AND no neurological deficit

- Non-contrast CT scan is the diagnostic test of choice
  - If CT is positive for SAH proceed to CT angiography or digital subtraction angiography.

Patient presented >6 hours from onset of symptoms OR presence of neurological deficit

- Non-contrast CT scan is the diagnostic test of choice
  - If CT is positive for SAH proceed to CT angiography or digital subtraction angiography.
  - If CT is negative for SAH, lumbar puncture (LP) should be performed to diagnose/exclude SAH
- Diagnosis of SAH is described in Figure 54-2


Subarachnoid hemorrhage diagnosis
Headache
Otawa criteria (any of the following)
Age ≥ 40 ys
Neck pain or stiffness
Withnessed loss of consciouness
Onset during exertion
Thunderclap headache
Limited neck flexion
6 HRS
< 6 hours AND no new neurological deficit
6 HRS
> 6 hours OR new neurological deficit
Non-contrast CT brain
Non-contrast CT brain
No
SAH diagnosed
Yes
Yes
SAH diagnosed
No
Lumbar puncture
Yes
Xanthochromia
No
Workup at physician discretion
Workup at physician discretion
CTA/DSA

Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2023 ;54:e314-e370

SAH: subarachnoid hemorrhage, CTA: CT angiography, DSA: digital subtraction angiography,

Figure 54-2: Diagnosis of SAH

Severity assessment of SAH

Scoring for severity assessment

- In patients with SAH, use of clinical scales (eg, the Hunt and Hess [HH] grade or World Federation of Neurosurgical Societies [WFNS] grade) is recommended to determine initial clinical severity and predict outcome.
- High-grade SAH include HH grade 4 and 5 or WFNS grade 4 and 5
- HH and WFNS scores are described in Table 54-1

Table 541: Scoring Systems for Assessment of Severity of SAH

Grade	WFNS	Hunt Hess
1	**GCS 15**	**Asymptomatic, mild headache, slight nuchal rigidity**
2	**GCS 13-15 without neurological deficit**	**Moderate to severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy**
3	**GCS 13-15 with neurological deficit**	**Drowsiness / confusion, mild focal neurologic deficit**
4	**GCS 7-12**	**Stupor, moderate-severe hemiparesis**
5	**GCS 3-6**	**Coma, decerebrate posturing**

Initial management

- Management of patients with SAH include prevention of early brain injury, delayed brain injury and general management.
- The management is described in Figure 54-3

General Measures

- Bed rest with elevation of the head to 20-35 degree
- Mild sedation/anxiolysis for grade I and II patients
- Agitation/delirium:
  - Haloperidol (Haldol) 2.5-5 mg IV PRN and then q 2-4 as required. Check QTc interval
  - Quetiapine (Seroquel) 25-50 mg BID (oral)
  - Dexmedetomidine infusion
- Pain
  - Paracetamol 1 g every 6-8 hrs
  - Fentanyl 25-50 ug q 4 PRN IV
  - Morphine 2-4 mg q 4 PRN IV
- Fever
  - Exclude infective causes of fever
  - Blood culture, chest x-ray, urine analysis and culture, CSF, sputum culture as appropriate
  - Serum CRP or procalcitonin
  - It should be treated aggressively and should be kept below 37.5 ºC
  - Paracetamol 1 g every 6-8 hrs
  - ibuprofen 300-800 mg TID (NOT contraindicated in SAH)
  - Active cooling
- Fluid management
  - Keep patients euvolemic
  - Good evidence supporting hypervolemia to prevent vasospasm DOES NOT exist
  - Start IV 0.9% NaCl @100ml/hrto be adjusted according to cardiac, pulmonary, and renal status
- DVT prophylaxis
  - SAH induces a prothrombotic state that may lead to an increased risk of DVT and PE

  - Sequential compression devices are recommended on admission
  - Prophylactic heparin 5,000 u s/c q 12, LMWH or fondaparinux are recommended 48–72 h after securing aneurysm
  - Seizures prophylaxis

Management of early brain injury

Avoidance of Rebleeding

Blood pressure management

- Initial blood pressure control with short-acting anti-hypertensive until aneurysm is secured.
- Insufficient evidence to suggest a specific blood pressure goal. Blood pressure management < 160-180 mmHg may be reasonable.
- Gradual blood pressure decrease if initial blood pressure > 180 mmHg with strict avoidance of hypotension (MAP < 65 mmHg).

Antifibrinolytic & antithrombotic reversal drugs

- No benefit of use of antifibrinolytic to improve functional outcome.
- Emergence reversal of anticoagulants in patients who are receiving anticoagulation.

Management of hydrocephalus

- In patients with SAH and acute symptomatic hydrocephalus, urgent CSF diversion (external ventricular drain (EVD) and/or lumbar drainage) should be performed to improve neurological outcome
- In patients with SAH and associated chronic symptomatic hydrocephalus, permanent CSF diversion is recommended to improve neurological outcome.

Management of seizures

- EEG monitoring is indicated in:
  - Fluctuating neurological examination,
  - Depressed mental state
  - Ruptured MCA aneurysm
  - High-grade SAH,
  - ICH,
  - Hydrocephalus,
  - Cortical infarction
- Prophylactic anticonvulsant is indicated in high-seizure-risk
  - Ruptured MCA aneurysm,
  - High-grade SAH,
  - ICH,
  - Hydrocephalus
  - Cortical infarction
- Prophylactic anticonvulsant is continued for ≤7 days.
- Phenytoin is not recommended for anti-seizure prophylaxis in SAH.

Management of delayed brain injury

Delayed cerebral ischemia (DCI) and vasospasm

- Cerebral vasospasm is defined as narrowing of cerebral arteries after SAH, which often begins 2-4 days following SAH, and lasts for up to 21 days
- Cerebral vasospasm can lead to decreased cerebral blood flow, resulting in DCI with neurological deficit related to prognosis in patients with SAH.
- Therefore, cerebral vasospasm must be treated as a clinical diagnosis along with radiological diagnosis, based on the neurological symptoms after SAH.

Diagnosis of vasospasm

Clinical diagnosis

- Change in mentation or focal deficit.

Investigation

- Transcranial Doppler (TCD): measures mean velocity and calculate Lindegaard ratio. Table 54-2
- Continuous EEG monitoring for detecting DCI and seizure activities
- CT angiography and digital subtraction angiography to detect vasospasm

Table 54-2: Transcranial Doppler criteria for vasospasm of middle cerebral artery and basilar artery

Severity of vasospasm of MCA	MFV (cm/s)	MFVMCA/MFVE$_{\text{ICA}}$ (Lindegaard ratio)
Hyperemia	**< 120**	< 3
Mild	120-149	3-6
Moderate	150-200	3-6
Severe	>200	**>6**
Severity of vasospasm of BA	**MFV (cm/s)**	**MFVBA/MFVEVA (Lindegaard ratio)**
Hyperemia	< 70	<2
Mild	70-85	≥2
Moderate	>85	>2.5
Severe	>85	>3

MCA; middle cerebral artery, MFV; mean flow velocity, EICA; extracranial internal carotid artery, BA; basilar artery, EVA; extracranial vertebral artery.

Prevention of vasospasm

Intravenous nimodipine (NOT FDA approved)

- Nimodipine can be given intravenously via a central venous catheter at a starting dose of 1 mg/hr (15 mcg/kg per hour, equivalent to 5 ml per hour) for the first 2 hours. If the patient tolerates the drug well and has no hypotension, the dose can be increased to 2 mg per hour (30 mcg/kg per hour, equivalent to 10 ml per hour) after the first 2 hours.

- If the patient's body weight is less than 70 kg or has hypotension, nimodipine should be started at a dose of 0.5 mg per hour (2.5 ml of solution per hour) or less, if necessary.

Oral nimodipine

- Dose: 60 mg oral/4 hours for 21 days
- Dose can be adjusted to 30 mg/2 hrs or 15 mg/1 hr to minimize hypotension.

Euvolemia

- Maintaining euvolemia can prevent vasospasm and DCI
- No role for prophylactic hemodynamic augmentation to prevent vasospasm.

Treatment of vasospasm

- Hemodynamic augmentation: Elevate blood pressure and ensure euvolemia
- Endovascular management and use of intra-arterial vasodilator with or without angioplasty to reverse vasospasm.

Hyponatremia

- Hyponatremia is a frequent complication in SAH because of either SIADH or cerebral salt losing syndrome.
- Fludrocortisone is used to treat hyponatremia after SAH

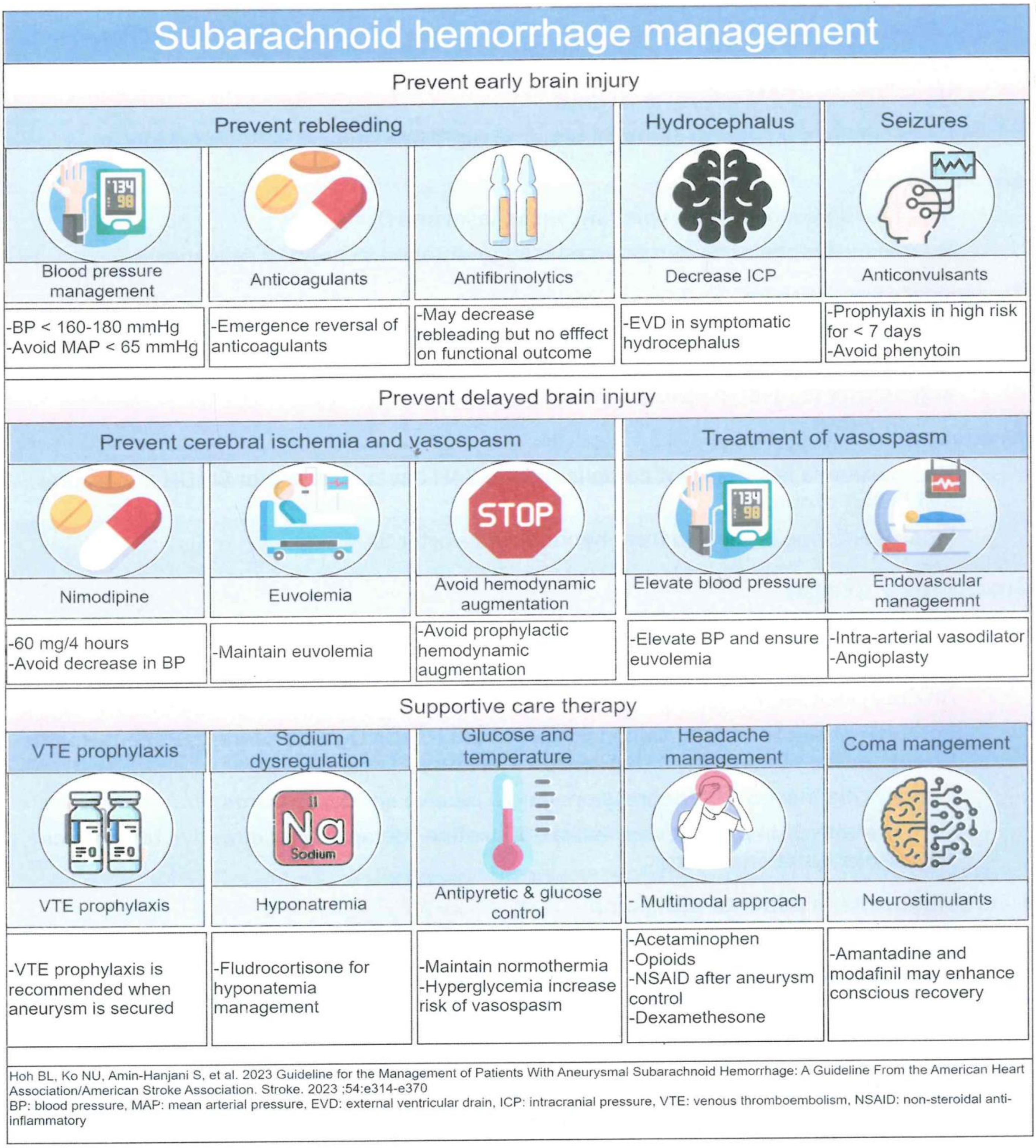
Recovery stage

Screening for depression and cognitive dysfunction

- Screening tools for anxiety include: Hospital Anxiety Depression Scale and General Anxiety Disorder-7
- Screening tools for depression include: Patient Health Questionairre-2, Patient Health Questionairre-9, and Beck's Depression Inventory
- Patients diagnosed with depression should receive antidepressants
- Patients with SAH without depression, fluoxetine therapy is not effective to enhance poststroke functional status.

Neurostimulants in patients with coma

- Early use of neurostimulants may be reasonable to promote consciousness recovery.
- Amantadine and modafinil can be used as neurostimulants in patients with SAH



Subarachnoid hemorrhage management

Prevent early brain injury

Prevent rebleeding			Hydrocephalus	Seizures
Blood pressure management	Anticoagulants	Antifibrinolytics	Decrease ICP	Anticonvulsants
-BP < 160-180 mmHg -Avoid MAP < 65 mmHg	-Emergence reversal of anticoagulants	-May decrease rebleading but no efffect on functional outcome	-EVD in symptomatic hydrocephalus	-Prophylaxis in high risk for < 7 days -Avoid phenytoin

Prevent delayed brain injury

Prevent cerebral ischemia and vasospasm			Treatment of vasospasm	
Nimodipine	Euvolemia	Avoid hemodynamic augmentation	Elevate blood pressure	Endovascular manageemnt
-60 mg/4 hours -Avoid decrease in BP	-Maintain euvolemia	-Avoid prophylactic hemodynamic augmentation	-Elevate BP and ensure euvolemia	-Intra-arterial vasodilator -Angioplasty

Supportive care therapy

VTE prophylaxis	Sodium dysregulation	Glucose and temperature	Headache management	Coma mangement
VTE prophylaxis	Hyponatremia	Antipyretic & glucose control	- Multimodal approach	Neurostimulants
-VTE prophylaxis is recommended when aneurysm is secured	-Fludrocortisone for hyponatemia management	-Maintain normothermia -Hyperglycemia increase risk of vasospasm	-Acetaminophen -Opioids -NSAID after aneurysm control -Dexamethesone	-Amantadine and modafinil may enhance conscious recovery

Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2023 ;54:e314-e370

BP: blood pressure, MAP: mean arterial pressure, EVD: external ventricular drain, ICP: intracranial pressure, VTE: venous thromboembolism, NSAID: non-steroidal anti-inflammatory

Figure 54-3: Management of SAH

References

1. Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2023;54:e314-e370.

Chapter 55

Management of Patients with Intracerebral Hemorrhage

General Principles

- Intracerebral hemorrhage (ICH) is a medical emergency
- Early deterioration is common and more than 20% of patients will experience a decrease in the Glasgow Coma Scale (GCS) of 2 or more points within the first few hrs.
- ICH score is a severity score that should be done routinely during early evaluation of these patients
- Management should include hemorrhage characteristics, medical management, and surgical management
- General approach for management of ICH is described in Figure 55-1

Initial Workup

- Focused neurologic exam (5 minutes): GCS
- History and types of anticoagulants
- Time of onset
- Patient's blood pressure
- Labs:
  - » Capillary glucose
  - » CBC
  - » PT/PTT, INR
  - » Creatinine
- Non-contrast CT
  - » ICH should be differentiated from hemorrhagic transformation
  - » CT finding of mass effect
  - » Sign of intraventricular expansion
  - » Signs of hydrocephalus
- CT angiography to diagnose the cause of ICH if the risk of macrovascular cause is high
  - » High risk patients
    - Young patient (< 50 years)
    - No history of hypertension
    - Lobar location
    - No CT signs of small vessels disease
    - Primary intraventricular hemorrhage
- Hemorrhage volume:
  - » Formula for estimating ICH hematoma volume is described in Figure 55-1
  - » Calculation of ICU score is described in Table 55-1.

Table 55-1: ICH score

Component	Criteria	Points
CGS	3 - 4 5 -12 13 -15	2 1 0
ICH Volume	≥ 30 ml < 30 ml	1 0
Intraventricular hemorrhage	Yes No	1 0
Infratentorial origin	Yes No	1 0
Age	≥ 80 years < 80 years	1 0
Total	**0 - 6**	
ICH score	**Mortality rate**	
0	0%	
1	13%	
2	26%	
3	72%	
4	94%	
5	100%	
6	**100%**	

Medical Management

Blood pressure management

- Keep systolic blood pressure ≤ 140 mm Hg
- The recommended agents that are used to lower blood pressure in patient with ICH are described in Table 55-2

Table 55-2:Agents used to lower blood pressure in patients with ICH.

Drug	Dose	Site of action	Side effects	Contraindications
Labetalol	0.25-0.5 mg/kg i.v. bolus or 2-4 mg/min i.v. infusion, thereafter 5-20 mg/h	Non-selective a1&8 blocker	Symptomatic postural hypotension, Flushing, Acute left ventricular failure	Asthma, Heart failure, Second- or third-degree heart block, Cardiogenic Shock,
Nicardipine	5 mg/h continuous i.v. infusion, increase dose by 2.5 mg/h every 15 min to a maximum dose of 15 mg/h	Ca-channel blocker (arterial dilator)	Dizziness, Flushing, Reflex tachycardia,	Liver failure
Clevidipine	1-2 mg/h i.v. infusion, increase every 2 min with 2 mg/h i.v. bolus or 15-30 mg/min continuous i.v. infusion	Ca-channel blocker (arterial dilator)	Systemic hypotension, Reflex tachycardia	Allergies to soybeans, soy products, eggs or egg products, Defective lipid metabolism, Severe aortic stenosis
Nitroprusside	0.25-10 pg/kg/min continuous i.v. infusion, increase by 0.5 pg/kg/min every 5 min to a maximal dose only for 10 min	Nitric oxide donor (Arterial and venous dilator)	Thiocyanate intoxication, Methemoglobinemia acidosis, Cyanide poisoning	Concurrent use with PDE-5 inhibitors, Vitamin B12 deficiency
Phentolamine	0.5-1 mg/kg i.v. bolus or 50-300 pg/kg/min continuous i.v. infusion	Non-selective a-blocker	Tachyarrhythmias, Orthostatic hypotension, Chest pain	

Anticoagulant reversal

- Anticoagulants reversal is described in Table 55-3

Warfarin reversal using FFP or PCC

- Decide on target INR
- Convert INR to percent (%) functional prothrombin complex (Table 55-4).
- Calculate the dose: (Target in %PC - Current level in %PC) X weight (kg) = mL of FFP or IU of PCC needed)
- Example: a patient with INR on arrival = 7.5, target INR 1.5, body weight = 80 kg: (40-5) X 80 = 2,800
- the needed dose is 2,800 mL of FFP or 2,800 IU of PCC

Table 55-3: Anticoagulant reversal in acute intracerebral hemorrhage

Anticoagulants	Reversal strategy	Rationale
Warfarin	• Stop warfarin immediately and check the INR • Vitamin K 10 mg intravenous infusion (slow-acting), monitor for anaphylaxis. • Four-factor prothrombin complex concentrate with INR-based dosing. • Repeat INR every 3–6 hours	• Prothrombin complex concetrate is superior to fresh frozen plasma in normalising the INR for warfarin-associated ICH • Vitamin K administration, in addition, may help to prevent a later re-increase in INR
Dabigatran	• Stop dabigatran immediately, check thrombin time, activated partial thromboplastin time. • Consider oral-activated charcoal (50 g) if last intake is <4 hours and safe to administer to the patient. • Idarucizumab 2×2.5 g boluses intravenously if recent ingestion or prolonged laboratory clotting times (not recommended if the thrombin time is within the normal range).	• Idarucizumab, a humanised monoclonal antibody fragment, rapidly and safely reverses dabigatran anticoagulation
Factor Xa inhibitors (apixaban, rivaroxaban, edoxaban and betrixaban)	• Stop the agent immediately, check prothrombin time, anti-factor Xa activity. • Consider oral-activated charcoal (50 g) if last intake is <4 hours and safe to administer to the patient. • Andexanet alpha intravenous bolus and infusion, dosing dependent on the dose and last dose timing of the factor Xa inhibitor.	• Andexanet alpha, a recombinant inactive factor Xa decoy', rapidly and effectively reduces anti-factor Xa activity
Heparin	• Stop heparin infusion/low-molecular-weight heparin (LMWH) immediately, check activated partial thromboplastin time. • Protamine sulphate slow intravenous infusion, 1 mg per 100 units of heparin, if activated partial thromboplastin time is prolonged or heparin was administered within the previous 2 hours. • Max dose 50 mg, monitor for anaphylaxis.	• Protamine sulphate fully reverses the effect of unfractionated heparin but only partly neutralises the effect of LMWH; the same dosing strategy can be used, but the longer half-life of LMWH may require cautious repeat infusions.

Table 55-4: Conversion of INR to % Function of Prothrombin Complex

INR Range	
> 5	5%
4 - 4.9	**10%**
2.6 - 3.9	15%
2.2 - 2.5	20%
1.9 - 2.1	25%
1.7 - 1.8	30%
1.4 - 1.6	40%
1	**100%**

Management of seizures

- Do not administer anticonvulsants prophylactically
- Treat clinical seizures with benzodiazepines then anticonvulsants
- Consider EEG monitoring if the patient's level of consciousness is less than is likely to be explained by the size and location of the hemorrhage.

Surgical Management

- Supratentorial hematoma evacuation
  - » Patients with a GCS score 9-12
  - » Patients with delayed neurological deterioration
- Infratentorial hematoma
  - » posterior fossa hemorrhage with acute hydrocephalus or brainstem compression,
- Decompressive craniectomy
  - » large hematomas leading to significant midline shift
  - » Patients with refractory intracranial hypertension
- External ventricular drain
  - » Intraventricular hemorrhage with hydrocephalus

Table 55-4: Conversion of INR to % Function of Prothrombin Complex

INR Range	
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2.6 - 3.9	15%
2.2 - 2.5	20%
1.9 - 2.1	25%
1.7 - 1.8	30%
1.4 - 1.6	40%
1	**100%**

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  - » large hematomas leading to significant midline shift
  - » Patients with refractory intracranial hypertension
- External ventricular drain
  - » Intraventricular hemorrhage with hydrocephalus

Management of ICH

Baseline evaluation

History of anticoagulants
-Type of anticoaglants
-Dose of anticoagulant
-Timing of the recent dose

SBP
-Target systolic pressure 130-140 mmHg

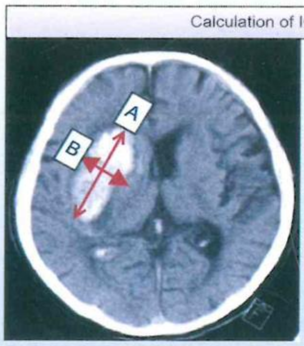
Assessment of severity
-ICH score

Lab investigations
-PT, PTT, INR
-CBC
-Serum creatinine

Imaging
-Non-contrast CT
-CTA to diagnose macrovascular cause

Assessment of severity

Calculation of ICH volume



A=Longest diameter

B=Longest diameter perpendiincular to A

C=Number of CT slices where hemorrhage is visible X slice thickness

Volume of ICH= (A X B X C)/2

ICH score calculation

GCS score	3-5	2
	5-12	1
	13-15	0
ICH volume	≥30	1
	< 30	0
Intraventricular hemorrhage	Yes	1
	No	0
Infratentorial origin	Yes	1
	No	0
Age	≥80	1
	< 80	0

ICH score interpretation

Total score	Mortality rate
0	0%
1	13%
2	26%
3	72%
4	94%
5-6	100%

Treatment

Blood pressure management

Immediate SBP<140 mmHg	Labetalol Nicardipine Alternative Nitroprusside

Reversal of anticoagulants

Warfarin	NOAC	Heparin

Surgical intervention

- Surgical evacuation in selected patient
- Decompressive craniectomy in hematoma with midline shift
- External ventricular drain in patient with hydrocephalus

McGurgan IJ, Ziai WC, Werring DJ, Al-Shahi Salman R,. Acute intracerebral haemorrhage: diagnosis and management. Pract Neurol. 2020;21:128–36

ICH: intracranial hemorrhage, CBC: complete blood count, CTA: CT angiography, GCS: glasgow coma score, NOAC: new oral anticoagulant, SBP: systolic blood pressure

Figure 55-1: Management of ICH

References

1. McGurgan IJ, Ziai WC, Werring DJ, Al-Shahi Salman R.. Acute intracerebral haemorrhage: diagnosis and management. Pract Neurol. 2020;21:128-36
2. Hemphill JC 3rd et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015;46:2032-60

Chapter 56

Status epilepticus

General Principle

- The Neurocritical Care Society Guidelines from 2012 defined status epilepticus (SE) as
    - Continuous electroclinical or electro-graphic seizures lasting for 5 minutes or more, or recurrent seizures without recovery to the patient's neurologic baseline between seizures
- The 2021 version of the ACNS's Standardized Critical Care EEG Terminology defines SE as
    - Electroclinical seizure lasting continuously for 10 minutes or more, or for a total duration of 20% or more of any 60-minute period of recording.
- Assessment and management of status epilepticus are described in Figure 56-1

Causes of status epilepticus

- Causes of SE can be classified as acute and chronic process (Table 56-1)

Table 56-1: Causes of status epilepticus

Acute processes	Chronic processes
• **Metabolic disturbance** • **Infection** • **CNS infection** • **Stroke** • **Head trauma** • **Drug toxicity/withdrawal** • **Non compliance with anti-epileptic drugs** • **Hypoxia** • **Cardiac arrest**	• **Pre-existing epilepsy** • **Anticonvulsant withdrawal** • **Chronic alcoholic tumor** • **CNS tumor** • **Organ failure**

- Medication that lower seizure threshold
    - Theophylline/Aminophylline
    - Carbapenems
    - Cefepime
    - Fluoroquinolones
    - Isoniazid
    - Antidepressant
    - Lithium
    - Cyclosporin

Complications of SE

- Hyperthermia
- Lactic acidosis
- Neurogenic pulmonary edema

- Rhabdomyolysis and AKI
- Hyperkalemia
- Aspiration
- Hypertension
- Hyper or hypoglycemia
- Permanent neurological damage

Diagnostic workup

- All patients
    - » CT brain
    - » CBC, Ca, Mg, Blood glucose
    - » EEG monitor
- Selected patient based on clinical presentation
    - » MRI brain
    - » Lumbar puncture
    - » Toxicology panel (Cocaine, theophylline, Organophosphates, cyclosporine, Tricyclic anti depressant
    - » Other lab: liver function tests, troponin, anticonvulsant level.

Management

Critical care treatment (dictated by clinical circumstances):

- Intubation for airway protection and mechanical ventilation
- Vital sign monitoring
- Peripheral IV access
- Treatment of hypotension with vasopressors
- Finger stick blood glucose
- Nutrient resuscitation (thiamine before dextrose)
- Hypertension may be related to ongoing seizure activity, and termination of status epilepticus often substantially corrects it.

Emergent initial therapy with benzodiazepines:

- Lorazepam 0.1 mg/kg IV, up to 4 mg per dose, may repeat once after 5-10 min
- Midazolam 10 mg IM if body weight > 40 kg, 5 mg if body weight 13-40 kg
- Diazepam 0.15-0.2 mg/kg, up to 10 mg per dose, may repeat once after 5 min

Urgent control therapy–antiseizure medications available in IV formulations

- Fosphenytoin/phenytoin 20 mg/kg IV, up to 1500 mg/dose
- Valproic acid 40 mg/kg IV, up to 3000 mg/dose
- Levetiracetam 60 mg/kg, up to 4500 mg/dose
- Phenobarbital 15 mg/kg IV
- Lacosamide 200-400 mg IV
- Midazolam 0.2 mg/kg IV bolus, followed by 0.05-2 mg/kg/h continuous infusion

- Antiseizure medications are described in Table 56-2

Refractory therapy

- Midazolam 0.2 mg/kg IV bolus, followed by 0.05–2 mg/kg/h continuous infusion
- Propofol 1–2 mg/kg IV bolus, followed by 20 pg/kg/min continuous infusion, titrate up to 30–200 pg/kg/min
- Pentobarbital 5–15 mg/kg IV bolus, may repeat 5–10 mg/kg IV bolus, followed by 0.5–5 mg/kg/h continuous infusion
- Antiseizure medications for refractory status epilepticus are described in Table 56-3

Prevent recurrence

- Prevention of seizure recurrence
- Management of precipitating causes

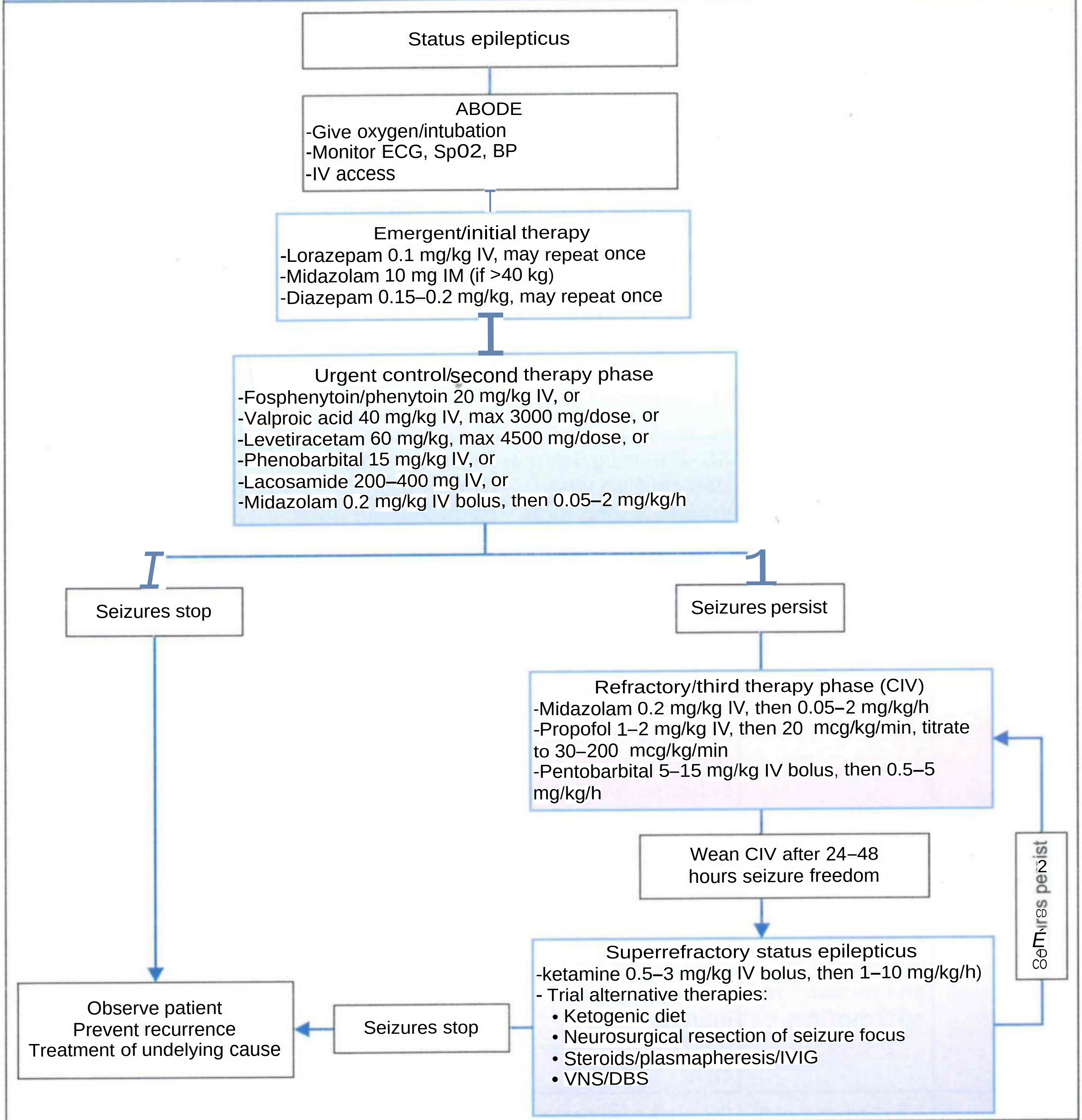
Treat complications

- Complications of status epilepticus are numerous and can involve multiple organ systems. In particular, convulsive status epilepticus is associated with
  - Cardiac complications such as hypertension and tachycardia
  - Rhabdomyolysis and hyperthermia.
  - Respiratory complications, including respiratory failure, hypoxia, and neurogenic pulmonary edema,
  - Neuronal damage and cerebral edema with increased intracranial pressure, which may require intracranial pressure monitoring and aggressive treatment with hypertonic agents.

Table 56-2: Antiepileptic drugs

Drug	Initial Dose	Administration Rate	Serious Adverse Effect	Consideration
Lorazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min	Up to 2 mg/min **(IVP)**	Hypotension Respiratory depression	Dilute 1:1 with saline IV contains propylene glycol
Midazolam	0.2 mg/kg IM up to maximum of 10 mg	Peds: 10 mg IM (>40 kg); 5 mg IM (13–40 kg); 0.2 mg/kg (intranasal); 0.5 mg/kg (buccal)	Respiratory depression Hypotension	Active metabolite, renal elimination, rapid redistribution (short duration)
Diazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min	Up to 5 mg/min (IVP) Ppds: 2–5 years, 0.5 mg/kg (PR); 6–11 years, 0.3 mg/kg (PR); greater than 12 years, 0.2 mg/kg (PR)	Hypotension Respiratory depression	Rapid redistribution (short duration), active metabolite, IV contains propylene glycol
Valproate Sodium	20–40 mg/kg IV, may give an additional 20 mg/kg	3–6 mg/kg/min, may give additional dose 10 min after loading infusion Peds: 1.5–3 mg/kg/min	Hyperammonemia Pancreatitis Thrombocytopenia Hepatotoxicity	Use with caution in patients with traumatic head injury; may be a preferred agent in patients with glioblastoma multiforme
Phenytoin	20 mg/kg IV, may give an additional 5–10 mg/kg	Up to 50 mg/min IV; may give additional dose 10 min after loading infusion	Arrhythmias Hypotension Purple glove syndrome	Only compatible in saline IV contains propylene glycol
Levetiracetam	1,000–3,000 mg IV Peds: 20–60 mg/kg IV	2–5 mg/kg/min IV		Minimal drug interactions Not hepatically metabolized
Lacosamide	200–400 mg IV	200 mg IV over 15 min, No pediatric dosing established	PR prolongation Hypotension	Minimal drug interactions Limited experience in treatment of SE
Topiramate	200–400 mg NG/PO	300–1,600 mg/day orally (divided 2–4 times daily) No pediatric dosing established	Metabolic acidosis	No IV formulation available

Management of status epilepticus


Status epilepticus
ABODE
-Give oxygen/intubation
-Monitor ECG, Sp02, BP
-IV access
Emergent/initial therapy
-Lorazepam 0.1 mg/kg IV, may repeat once
-Midazolam 10 mg IM (if >40 kg)
-Diazepam 0.15–0.2 mg/kg, may repeat once
Urgent control/second therapy phase
-Fosphenytoin/phenytoin 20 mg/kg IV, or
-Valproic acid 40 mg/kg IV, max 3000 mg/dose, or
-Levetiracetam 60 mg/kg, max 4500 mg/dose, or
-Phenobarbital 15 mg/kg IV, or
-Lacosamide 200–400 mg IV, or
-Midazolam 0.2 mg/kg IV bolus, then 0.05–2 mg/kg/h
Seizures stop
Seizures persist
Refractory/third therapy phase (CIV)
-Midazolam 0.2 mg/kg IV, then 0.05–2 mg/kg/h
-Propofol 1–2 mg/kg IV, then 20 mcg/kg/min, titrate to 30–200 mcg/kg/min
-Pentobarbital 5–15 mg/kg IV bolus, then 0.5–5 mg/kg/h
Wean CIV after 24–48 hours seizure freedom
Seizures persist
Superrefractory status epilepticus
-ketamine 0.5–3 mg/kg IV bolus, then 1–10 mg/kg/h)
- Trial alternative therapies:
• Ketogenic diet
• Neurosurgical resection of seizure focus
• Steroids/plasmapheresis/IVIG
• VNS/DBS
Seizures stop
Observe patient
Prevent recurrence
Treatment of undelying cause

McGurgan IJ, Ziai WC, Werring DJ, Al-Shahi Salman R,. Acute intracerebral haemorrhage: diagnosis and management. Pract Neurol. 2020;21:128–36
CIV, Continuous intravenous infusion; DBS, deep brain stimulation; EEG, electroencephalogram; IVIG, intravenous immune globulin; VNS, vagus nerve stimulation.

Figure 56-1: Status epilepticus management

Table 56-3: Pharmacological management of refractory status epilepticus

Drug	Initial Dose	Continuous Infusion	Serious Adverse Effect	Consideration
Midazolam	0.2 mg/kg intravenouly over 2 to 5 min repeat 0.2 to 0.4 mg/kg boluses every 5 minutes until seizures stop, up to a maximum loading dose of 2 mg/kg	0.05–2 mg/kg/hr Breakthrough SE: 0.1–0.2 mg/kg bolus, increase rate by 0.05–0.1 mg/kg/hr every 3–4 h	Hypotension Respiratory depression	Tachyphylaxis occurs after prolonged use Active metabolite, renally eliminated, rapid redistribution (short duration), does NOT contain propylene glycol
Propofol	Start at 20 mcg/kg/min, with 1–2 mg/kg loading dose	30–200 mcg/kg/min Use caution when administering high doses (>80 mcg/kg/min) for extended periods of time (i.e., >48 h) Peds: Use caution with doses > 65 mcg/kg/min; contraindicated in young children Breakthrough SE: Increase rate by 5–10 mcg/kg/min every 5 min or 1 mg/kg bolus plus Titration	Hypotension (especially with loading dose in critically ill patients) Respiratory depression Cardiac failure Rhabdomyolysis Metabolic acidosis Renal failure	Requires mechanical Ventilation Must adjust daily caloric intake (1.1 kcal/ml)
Thiopental	2–7 mg/kg, administer at an infusion rate ≤5 0 mg/min	0.5–5 mg/kg/h Breakthrough SE: 1–2 mg/kg bolus, increase rate by 0.5–1 mg/kg/h every 12 h	Hypotension Respiratory depression Cardiac depression	Requires mechanical Ventilation Metabolized to pentobarbital
Ketamine	1.5 mg/kg every 3 to 5 minutes until seizure stops, up to a maximum of 4.5 mg/kg	20 pg/kg/minutes (1.2 mg/kg/h; bolus and increase rate by 10–20 mg/kg/min until seizure control is established) (0.3–7.5 mg/kg/h)	it causes elevation of the blood pressure	Use with caution in patients with ocular injuries, hypertension, chronic congestive heart failure (CHF), Myocardial infarction (MI), tachyarrhythmias, and history of alcohol abuse

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Chapter 57

Paroxysmal Sympathetic Activity

General Principle

- Paroxysmal sympathetic activity (PSA) is a syndrome following acquired brain injury consisting of transient, paroxysmal and simultaneous increase in sympathetic nervous system function
- PSA affects one third of patients with TBI
- It occurs within 24 hours to weeks after brain injury
- PSA episode occurs 1 to 10 times per day and varies from 1 to 10 hours
- Syndrome duration from 1 to 2 weeks to several months

Symptoms

- Fever > 38.5 ºC
- Tachycardia (HR> 120 bpm or > 100 bpm if receiving beta blocker)
- Tachypnea (RR> 20/min)
- Hypertension (SBP> 160 mmHg)
- Diaphoresis
- Posturing
- Severe dystonia
- Rigidity

Differential Diagnosis

- Sepsis
- Encephalitis
- Seizures
- Hydrocephalus
- Drug withdrawal

Treatment Goals

- Reduce duration of episodes
- Lessen intensity of episodes
- Inhibiting central sympathetic outflow
- Inhibiting afferent sensory blocking
- Blocking end organ response of the sympathetic nervous system

Opioid Receptor Agonist

- Morphine dose: 2 to 8 mg from the onset of PSA episode then 1 to 2 mg every 1 to 2 hrs

Non- Selective Beta Blocker:

- Propranolol PO dose: 20 to 60 mg every 4-6 hours max 240 mg/ day
- Labetalol IV dose: 10 to 20 mg every hr (repeat every 10 min until BP is achieved) max 300 mg/day
- Goal: systolic BP < 160 mmHg
- Hold if HR< 60 bpm

Gamma-Aminobutyric Acid (GABA) A and B agonist

- GABA A :
  - » Benzodiazepine
  - » Midazolam 1 to 2 mg IV, lorazepam 2 to 4 mg IV, diazepam 5 to 10 mg IV
  - » Useful for patients with anxiety
- GABA B :
  - » Baclofen
    - Dose: 5 mg PO 3 times a day, Max 80 mg/day
    - Useful for relieving spasm , pain muscle rigidity
    - Abrupt withdrawal can lead to fever, rigidity, dystonia, or seizures
  - » Gabapentin
    - Dose: 300 to 900 PO mg/day, titrate up to 4800 mg/day
    - Well tolerated for long term use
    - Useful for acute and chronic phase as an adjunctive therapy

Alpha Adrenergic Agonist

- Clonidine dose: 0.2-0.6 mg/day in 2-3 divided dose; Max 2.4 mg/day
- Dexmedetomidine 0.2-0.7 mg/kg/hr as a continuous infusion
- Useful in treating hypertension and tachycardia
- Used instead of propranolol in patients with bronchial asthma

Dantrolene

- Dose: 0.25 to 2 mg/kg IV every 6 to 12 hrs; Max 10 mg/kg/day
- Useful for severe dystonia posturing
- Contraindicated in active liver disease

Dopamine Antagonists

- Haloperidol, chlorpromazine, atypical antipsychotics metoclopramide (NOT recommended)

References

1. Baguley IJ et al. Paroxysmal sympathetic hyperactivity after acquired brain injury: consensus on conceptual definition, nomenclature, and diagnostic criteria. *J* Neurotrauma. 2014;31:1515-20

Chapter 58

Neuromuscular disorder in critically ill patients

Guilliane-Barré syndrome (GBS)

General Principle

- Guilliane Barré syndrome [GBS) "also called acute inflammatory demyelinating polyradiculoneuropathy (AIDP)", is an inflammatory disorder affecting the peripheral nervous system that is characterized by acute or subacute onset and typically monophasic course of the disease.
- The pathogenesis of GBS is based on the autoimmune damage of the myelin sheath of the peripheral nerves
- These infections are most often caused by viruses (cytomegalovirus, Epstein- Barr, HIV, enteroviruses, herpes simplex, hepatitis A and C viruses) but also may be of bacterial origin (Mycoplasma or Campylobacter jejuni)

Symptoms

- **Sensory disturbance** is often the first symptom.
  - » Paresthesias are common, especially in the fingers and toes
  - » Pain can result from nerve root inflammation (e.g., in back or extremities, low back pain). Pain may be radicular or neuropathic.
  - » Sensory loss can occur, but this is mild compared to motor dysfunction.
- **Ascending flaccid paralysis.**
  - » Relatively symmetric.
  - » Speed of progression correlates with disease severity.
  - » The ascending pattern is thought to be due to nerve length, with longer nerves at higher risk of injury.
  - » 25% of patients develop weakness leading to respiratory failure.
- **Cranial nerve involvement .**
  - » Occasionally ocular, facial, or oropharyngeal muscles are affected first.
  - » Facial weakness, ophthalmoplegia.
  - » Difficulty swallowing.
- **Dysautonomia:**
  - » Blood pressure may be extremely labile.
  - » Sympathetic activation can occur (with hypertension, agitation, diaphoresis, tachycardia, vasoconstriction), which may be complicated by:
    - Posterior reversible leukoencephalopathy syndrome (PRES).
    - Takotsubo cardiomyopathy
  - » Parasympathetic activation can occur (with bradycardia, facial flushing, vasodilation).
  - » Other features may include constipation, diarrhea, and urinary retention.

Diagnostic test

- CSF analysis
    - Elevated protein (After one week)
    - Cell count < 50 mm3
- EMG and nerve conduction velocity
- MRI

General management

Hemodynamics

- Blood pressure swings are often short-lived, so avoid treatment when possible. Aggressive treatment of hemodynamic fluctuations may merely worsen the hemodynamic roller-coaster (e.g., initiation of a vasopressor during a hypotensive episode exacerbates a subsequent episode of hypertension).
- Avoid beta-blockers, as these may increase the risk of bradycardia.
- For persistent or critical hypotension:
    - Administer fluid if there is evidence of true hypovolemia (e.g., negative fluid balance, poor PO intake for days).
    - May use vasopressor, at the lowest dose possible.
- For persistent or critical hypertension:
    - Avoid treatment unless there is target-organ damage or ongoing severe hypertension (e.g., MAP > ~120 mm).
    - Avoid beta-blockers (these may aggravate subsequent bradycardia).
    - Short-acting vasodilator (e.g., nicardipine or clevidipine infusion).

Pain

- Gabapentin for neuropathic pain.
- Opioid is used with caution.

Specific management of GBS

- The first line of therapy may include treatment With intravenous immunoglobulin (IVIG) (0.4 g/kg/day for 5 days) or plasmapheresis, which are equally effective.
- IVIG has fewer side effects than plasma exchange (PE), which would favor IVIG over PE treatment.
- IVIG treatment after PE, as a standard combination, does not produce significant extra benefit and cannot be recommended.
- Combining high-dose intravenous methylprednisolone with IVIG may have a minor short-term benefit.
- Patients who improve after IVIg and then relapse should preferentially be retreated with a second course of IVIG
- In patients who seem to be unresponsive to the first course of IVIG, a second course may be tried, but evidence supporting such a strategy is lacking

Myathenia gravis

General Principle

- Myasthenia gravis is a consequence of the autoimmune attack on the acetylcholine receptor complex at the postsynaptic membrane of the neuromuscular junction.
- 20% of patients with myasthenia gravis develop myasthenic crisis with respiratory failure requiring mechanical ventilation.

Clinical presentation

- Myasthenia gravis typically involves ocular muscle weakness producing ptosis and diplopia, in addition to bulbar muscle weakness resulting in dysphagia and dysarthria.
- Drugs that may increase the weakness in myasthenia gravis are described in Table 58-1

Table 58-1: Drugs that may increase weakness in myasthenia gravis

- Neuromuscular blocking agents
- Selected antibiotics
  - » Aminoglycosides, particularly gentamicin
  - » Macrolides, particularly erythromycin and azithromycin
- Selected cardiovascular agents
  - » Beta-blockers
  - » Calcium channel blockers
  - » Procainamide
- Quinidine
- Quinine
- Corticosteroids
- Magnesium salts
  - » Antacids, laxatives, intravenous tocolytics
- Iodinated contrast agents
- d-Penicillamine

Treatment

Plasma exchange

- It usually causes improvement in a few days. It directly removes anti-acetylcholine receptor antibody from the body.
- The main advantage of plasma exchange is more rapid response compared to IVIG

Intravenous immunoglobulin (IVIG)

- IVIG takes longer to work (e.g., 2-3 weeks), but the efficacy may be more sustained.
- IVIG can be used in situations where plasma exchange is unavailable or contraindicated.
- The dose of IVIG is 2 grams/kg, usually divided over 2 or 5 days

Corticosteroids

- Corticosteroids (e.g., prednisone 1 mg/kg/day) are occasionally used in prolonged myasthenic crises that fail to respond to plasma exchange or IVIG

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2. Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012;78:1009-15
3. Roper J, Fleming ME, Long B, et al. Myasthenia Gravis and Crisis: Evaluation and Management in the Emergency Department. *J* Emerg Med. 2017;53:843-853

Chapter 59

Post resuscitation care

General principles

- Post resuscitation care guidelines are based on recent recommendation developed by The International Liaison Committee on Resuscitation (ILCOR).
- The guidelines include recommendations on the immediate management post return of spontaneous circulation, diagnostic investigations of the cause cardiac arrest, general intensive care management, and prognostication parameters
- The outline of recommendations is described in Figure 59-1

Immediate treatment

Airway and breathing

- Maintain Sp02 94%-98%
    - » Avoid hypoxemia and hyperoxemia
- Insert advanced airway
- Ventilation to normocapnia
    - » In patients requiring mechanical ventilation after ROSC, adjust ventilation to target a normal arterial partial pressure of carbon dioxide ($PaCO_2$), i.e.35–45 mmHg.

Circulation

- 12-lead ECG
- Obtain reliable IV access
- Aim systolic pressure> 100 mmHg
- Fluid is crystalloid. Restore normovolemia.
- Intra-arterial pressure monitoring
- Consider vasopressor/inotrope to maintains

Control temperature

- Maintain a target temperature at a constant value between 32 and 36 °C for at least 24 hrs.
- Avoid fever (> 37.7 °C) for at least 72 h after ROSC in patients who remain in coma.
- Sedation; control shivering.

Diagnosis

- Emergent cardiac catheterization and PCI for ST segment elevation
- Cardiac catheterization can be considered in patients with No ST segment elevation if there is high probability of acute coronary syndrome.
- Echocardiography to detect undelying cardiac pathology
- CT brain +/- CT angiography

ICU management

General management

- Use short acting sedatives and opioids.
- Avoid using a neuromuscular blocking drug routinely.
- Provide stress ulcer prophylaxis routinely in cardiac arrest patients.
- Provide deep venous thrombosis prophylaxis.
- Target a blood glucose of 140–180 mg/dL using an infusion of insulin if required; avoid hypoglycemia < 70 mg/dL
- Start enteral feeding at low rates (trophic feeding) during TTM and increase after rewarming if indicated. If TTM of 36 °C is used as the target temperature, gastric feeding rates may be increased early during TTM.
- Prophylactic antibiotics is not recommended routinely.
- Treatment of seizures with sodiufn valproate or levetiracetam as first line of therapy

Hemodynamic management

- Systolic blood pressure > 100 mmHg or mean arterial pressure > 65 mmHg
- Target is maintaining urine output ≥ 0.5 ml/kg/hr and and normalizing serum lactate
- IV crystalloid, norepinephrine +/- dobutamine according to volume status and cardiac function
- Maintain SP02 94–98% or Pa02 is around 100 mmHg
- Do not treat bradycardia during TTM at 33 °C if blood pressure, lactate, $SCVO_2$ or SVO_2 are adequate. If not, consider increasing the target temperature, but to no higher than 36 °C.
- Do not give steroids routinely after cardiac arrest.
- Consider mechanical circulatory support (intra-aortic ballon, ventricular assisted device in cardiogenic shock with persistent hemodynamic instability.

Targeted temperature management

- Targeted temperature management protocol is described in Table 59-1

Prognostication

- Start the prognostication assessment after major confounders (e.g. residual sedation, hypothermia) have been excluded
- Indication to perform multimodality prognostication test:
  - A Glasgow Motor Score of ≤ 3 (abnormal flexion or worse in response to pain) at 72 hrs or later after ROSC
- Tests that predict poor outcome (At least 2 of the followings)
  - No pupillary and corneal reflex at ≥ 72 hrs
  - Bilateral absent N20 somatosensory evoked potential wave
  - Highly malignant EEG at ≥ 24 hrs
  - suppressed background with or without periodic discharges and burst-suppression.
  - Neurone specific enolase > 60 pg/L at 48 and/or 72 hrs

Complications

- bradycardia
- hypotension
- decreased cardiac output
- Atrial Fibrillation is common
- severe dysrhythmias are more common below 30°C (86°F)
- Other ECG changes in hypothermia include prolongation of the PR, QRS and QT intervals
- hypophosphatemia, hypomagnesemia, hypocalcemia or hypokalemia.
- hyperglycemia by decreasing insulin sensitivity and secretion

Laboratory Tests

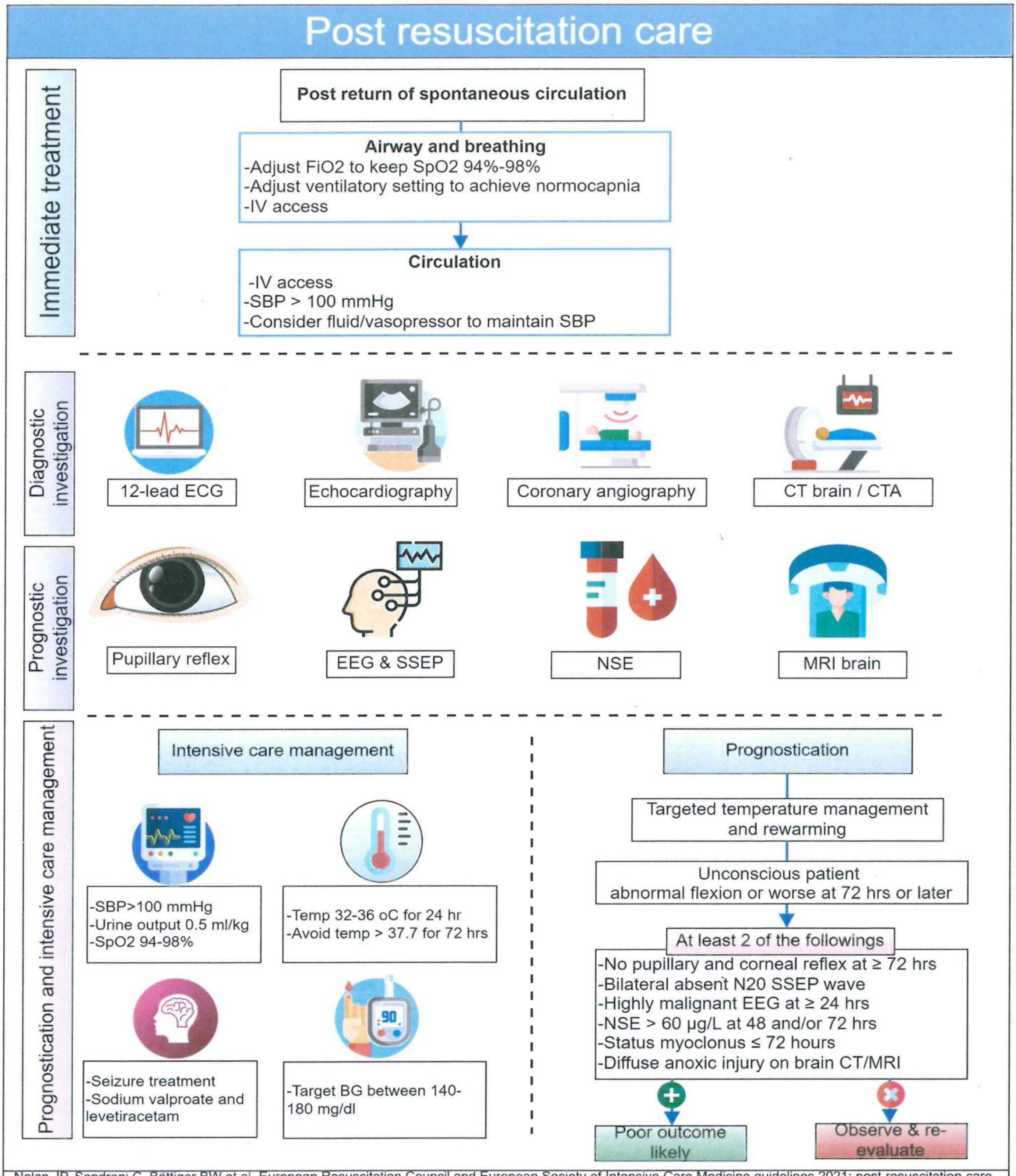
- Potassium and magnesium levels fall (should be corrected)
- low WBC, high PT/APPT and LFTs (do not require treatment)
- Blood gas analysis may show low pH and HC03- and high pC02 and p02
- Drug metabolism is generally slowed, leading to increased half-life, and hence drug accumulation

Shivering Prevention

- Wrap head, hand, and feet with blanket.
- Magnesium 4 g bolus over 4 hrs

Shivering Treatment

- Fentanyl 50 ug bolus
- Increase basal sedation (Propofol or midazolam)
- Bolus neuromuscular blocking agent followed by continuous infusion if needed



Post resuscitation care

Immediate treatment

Post return of spontaneous circulation

Airway and breathing
- -Adjust FiO2 to keep SpO2 94%-98%
- -Adjust ventilatory setting to achieve normocapnia
- -IV access

Circulation
- -IV access
- -SBP > 100 mmHg
- -Consider fluid/vasopressor to maintain SBP

Diagnostic investigation

- 12-lead ECG
- Echocardiography
- Coronary angiography
- CT brain / CTA

Prognostic investigation

- Pupillary reflex
- EEG & SSEP
- NSE
- MRI brain

Prognostication and intensive care management

Intensive care management

-SBP>100 mmHg
-Urine output 0.5 ml/kg
-SpO2 94-98%

-Temp 32-36 oC for 24 hr
-Avoid temp > 37.7 for 72 hrs

-Seizure treatment
-Sodium valproate and levetiracetam

-Target BG between 140-180 mg/dl

Prognostication

Targeted temperature management and rewarming

Unconscious patient
abnormal flexion or worse at 72 hrs or later

At least 2 of the followings
- -No pupillary and corneal reflex at ≥ 72 hrs
- -Bilateral absent N20 SSEP wave
- -Highly malignant EEG at ≥ 24 hrs
- -NSE > 60 μg/L at 48 and/or 72 hrs
- -Status myoclonus ≤ 72 hours
- -Diffuse anoxic injury on brain CT/MRI

+ Poor outcome likely

✕ Observe & re-evaluate

Nolan JP, Sandroni C, Böttiger BW et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med. 2021;47:369-421

FiO2: fraction of inspired oxygen, SpO2: oxygen satuation, SBP: systolic blood pressure, MRI: magnetic resonance imaging, EEG: electroencephalography, NSE: neuron specific enolase, SSEP: somatosensory evoked potential, BG: blood glucose

Figure 59-1: Post cardiac arrest algorithm

References

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SECTION 13

Management of Burn

Chapter 60

Critical Care of Burn Patient

General principles

- The inflammatory responses to burn injury cause multiorgan failure and early death without adequate resuscitation.
- The patient's optimal chance for survival and a meaningful recovery depends upon appropriate fluid resuscitation, airway management, and appropriate, timely burn care.
- Management of burn can be summarized in Figure 60-1

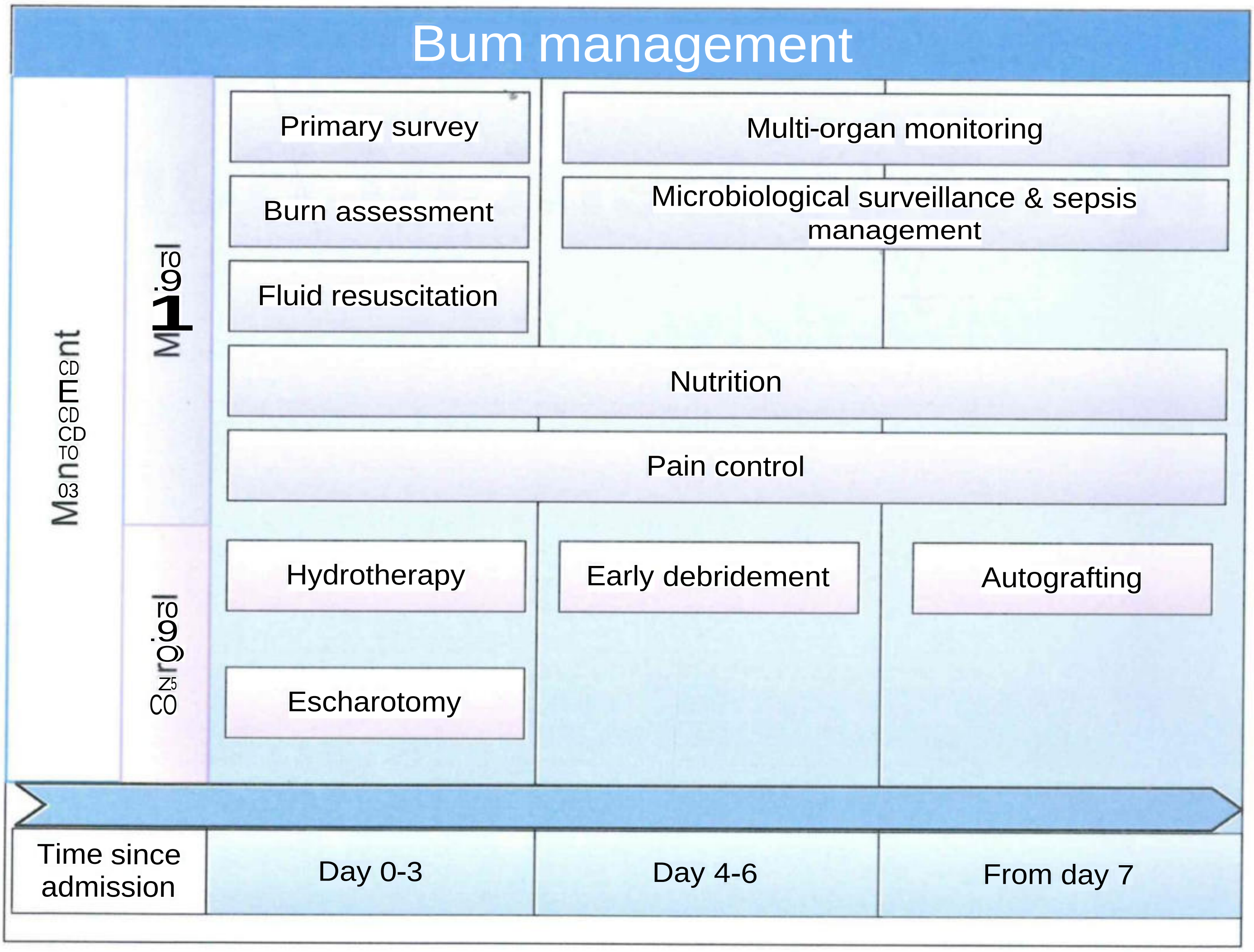

Burn management
Management
Medical
Surgical
Primary survey
Burn assessment
Fluid resuscitation
Multi-organ monitoring
Microbiological surveillance & sepsis management
Nutrition
Pain control
Hydrotherapy
Escharotomy
Early debridement
Autografting
Time since admission
Day 0-3
Day 4-6
From day 7

Figure 60-1:Burn management

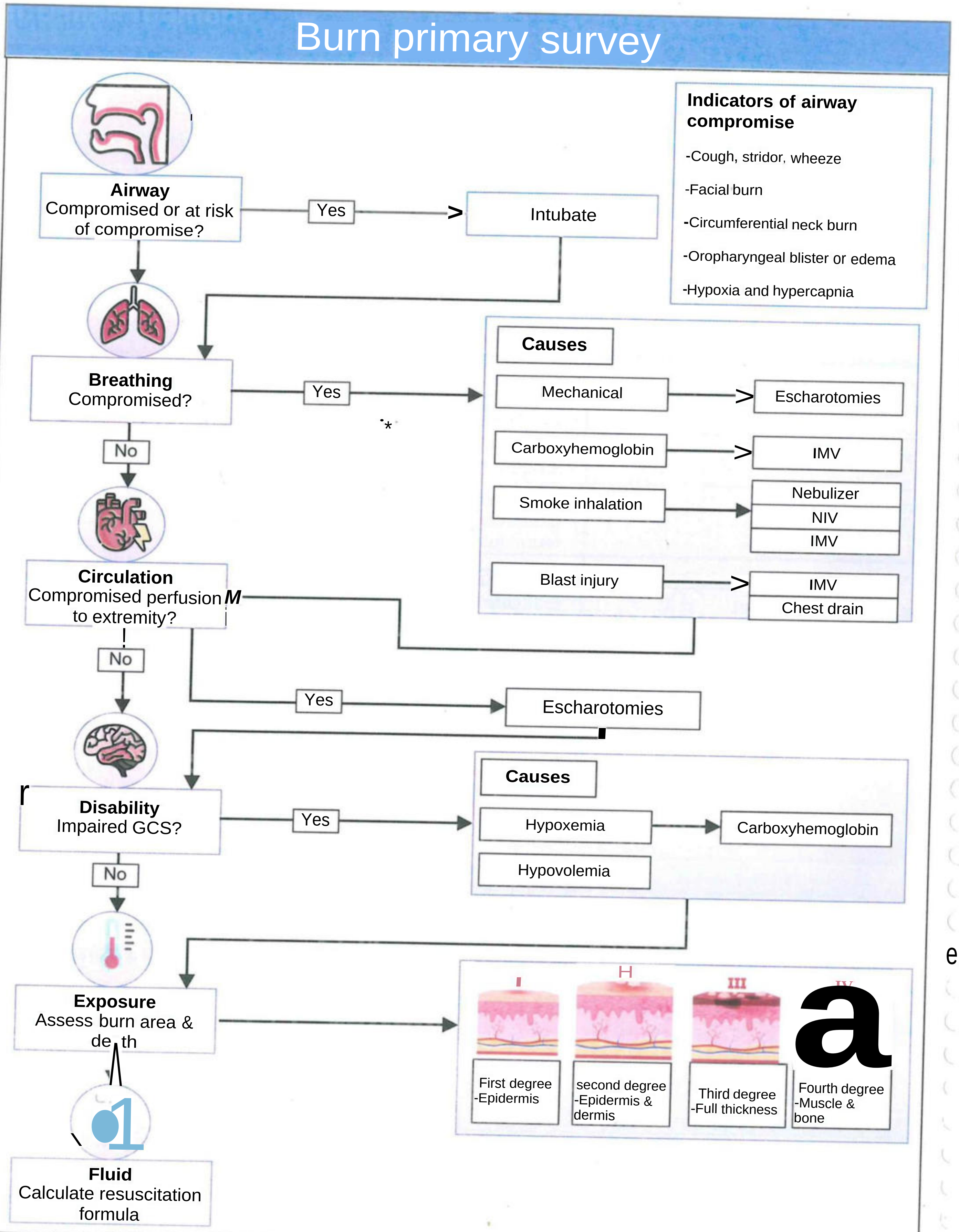
Primary Survey:

- Burn primary survey is similar to any trauma survey that includes assessment of airway, breathing, circulation, disability, and exposure
- Early intubation of burn patient should be considered when the airway is compromised or at risk of compromise.

  - Facial burn
  - Cough, stridor, or wheezes
  - Oropharyngeal blister of edema
  - Hypoxia and/or hypercapnia
  - Circumferential neck burn
- Patient with suspected inhalational injury should be suspected to have carbon monoxide poisoning and need assessment using cooximeter.
- Burn primary survey is described in Table 60-1 & Figure 60-2

Table 60-1: Burn primary survey

Primary survey	Management
Airway	• **Stabilize cervical spine.** • **Cjieck airway patency.** • **Observe for signs of inhalation injury.**
Breathing	• **Humidified oxygen should be commenced. If breathing is compromised, consider early endotracheal intubation.**
Circulation	• **Check pulses and blood pressure. Consider IV access** • **Circumferential deep dermal to full thickness burns may cause a tourniquet effect. Escharotomies may be required.**
Disability	• **Assess conscious state.**
Exposure/environment	• **Estimate percent of total body surface area burned (%TBSA). Monitor temperature, avoid hypothermia.**
Brief history	• **Allergies, past medical history, tetanus status, medications and last meal**


Burn primary survey
Airway
Compromised or at risk of compromise?
Yes
Intubate
Indicators of airway compromise
-Cough, stridor, wheeze
-Facial burn
-Circumferential neck burn
-Oropharyngeal blister or edema
-Hypoxia and hypercapnia
Breathing
Compromised?
Yes
No
Causes
Mechanical
Eschartomies
Carboxyhemoglobin
IMV
Smoke inhalation
Nebulizer
NIV
IMV
Blast injury
IMV
Chest drain
Circulation
Compromised perfusion to extremity?
No
Yes
Escharotomies
Disability
Impaired GCS?
Yes
No
Causes
Hypoxemia
Carboxyhemoglobin
Hypovolemia
Exposure
Assess burn area & depth
I
II
III
IV
First degree
-Epidermis
second degree
-Epidermis & dermis
Third degree
-Full thickness
Fourth degree
-Muscle & bone
Fluid
Calculate resuscitation formula

Hettiaratchy S, Papini R. Initial management of a major burn: I--overview. BMJ. 2004 Jun 26:328(7455):1555-7
GCS:Glasgow coma scale,

Figure 60-2: Burn primary survey

Colloid infusion

- Albumin 5% or fresh frozen plasma is indicated in
  - Total infused volume > 250 ml/kg
  - Persistent oliguria
- The rate of albumin 5% infusion depends on TBSA % as described in Figure 60-3

Resuscitation endpoints in the first 24 hours post-burn injury:

- Monitor arterial lactate q 4 hours until < 2 mMol/L
- Maintain urine output at 30-50 ml/hr
- In electrical injury or rhabdomyolysis patients, serial creatinine kinase levels should be checked daily until < 2500 mcg/L
- Monitor hemoglobin to ensure that it is not trending upward.

Fluid resuscitation in pediatric patient < 30 kg

- Fluid resuscitation protocol is described in Figure 60-3

Modified brooks formula

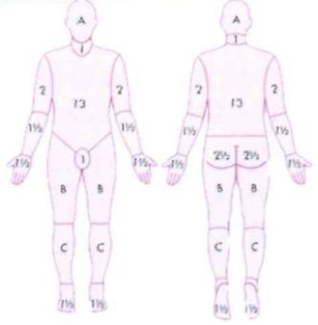
- 3 mL/kg/% TBSA burned. Fluid replacement is required in patients with burns ≥ 20% TBSA.
  - Give ***Zi*** of the fluid volume calculated over the first 8 hours from the time of the burn.
  - Give the remaining half of the fluid volume over the next 16 hours.
- Maintenance fluid containing dextrose (D5% 0.45 NaCl) according to the 4:2:1 rule
  - (1-10 kg x 4) + (11-20 kg x 2) + (-20 kg x 1) mL/h

Lactated ringer solution	**Example:** **12 kg child with 40% TBSA burned**
• 3ml x % of burn x body weight (kg) = quantity over 24 hours • Give 50% of the fluid in the first 8 hours • Give 50% of the fluid in the next 16 hours	• 3x40%x12kgs=1440 mis • 720mls in 8 hours (90 ml/hr) • 720mls in 16 hours (45 ml/hr)
Maintenance fluid	
D5% + 0.45% Normal Saline	**Example: 12 kg**
• 4mls/kg/Hr for the first kg • 2mls/kg/Hr for between 10 - 20 kg • 1mls/kg/Hr for greater than 20kg	• 4mls per kg for the first 10kg=40mls • 2mls/kg for between 10-20kg=4mls • Total=44 ml/hr to be added to calculated parkland formula

Burn resuscitation

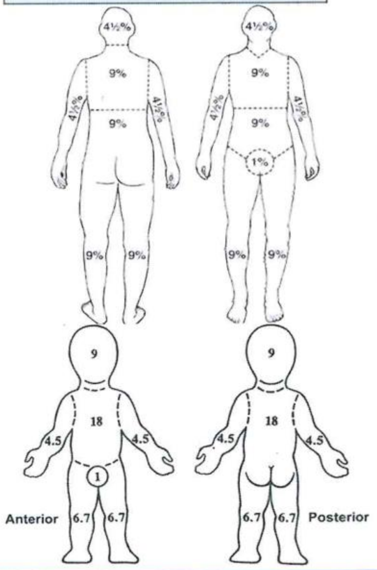
Calculate TBSA %

Lund-Browder chart



Area	0	1	5	10	15	Adult
A=1/2 of head	9.5	8.5	6.5	5.5	4.5	3.5
B=1/2 of one thigh	2.75	3.75	4	4.5	4.5	4.75
C=1/2 of lower leg	2.5	2.5	2.75	3	3.25	3.5

Rule of 9 chart



Calculate resuscitation volume (LR)

Adult burn > 20% TBSA

Parkland formula
4 ml/kg/TBSA%
1/2 in first 8 hrs
1/2 in second 16 hrs

Rule of 10
10 X TBSA% for 40-80 kg
+
10 X kg for > 80 kg

70 kg patient (50% burn)

4X70X50=1400 cc
1st 8 hrs=7000/8=875 ml/hr
2nd 16 hrs=7000/16=437 ml/hr

10X50=500 ml/hr

Pediatric burn > 15% TBSA

Modified brooks formula
3 ml/kg/TBSA%
1/2 in first 8 hrs
1/2 in second 16 hrs

Maintenance fluid
4:2:1 rule
(1–10 kg x 4) + (11–20 kg x 2) + (>20 kg x 1) mL/h

Adjust resuscitation volume each hour

Urine output

<0.25 ml/kg	0.25-0.5 ml/kg	0.5-1 ml/kg	1-2 ml/kg	>2 ml/kg
↑ rate by 20%	↑ rate by 10%	Maintain the same rate	↓ rate by 10%	↓ rate by 20%

Assess resuscitation after 12 hours

Warning sign
- Infused volume> 250 ml/kg over 24 hours
- Urine output < 0.5 ml/kg
- MAP < 65 mmHg

⇨

Colloid infusion in adult

TBSA (%)	30%-49%	50%-69%	>70%
Albumin 5% rate (ml/hr)	50	100	150

Shock refractory to fluid titration

Vasopressin Norepinephrine	Replace calcium Hydrocortisone	Check missed injuries

Causbie, J.M.; Sattler, L.A.; Basel, A.P.; Britton, G.W.; Cancio, L.C. State of the Art: An Update on Adult Burn Resuscitation. Eur. Burn J. 2021, 2, 152-167

TBSA: total body surface area burned, MAP: mean arterial pressure, LR: lactated ringer.

Figure 60-3: Burn resuscitation protocol

Nutritional management:

Energy requirements

- Energy expenditure needs to be assessed using indirect calorimetry
- In case of absence of indirect calorimetry, predictive equation can be used.
- Toronto equation seems to be the most suitable one in adult, since it estimates the energy required together with course of the disease.
  - » Toronto equation = (-4343+[10.5 X % TBSA]+[0.23 X caloric intake]+[0.84 X REE by Harris-Benedict]+[114 X rectal temperature in °C]-[4.5 X day post burn])
- Schoffield equation is the equation of choice in pediatric patients
  - » Girls (3-10 ys)= (16.97 X weight in kg)+ (1.618 X height in cm)+371.2
  - » Boys (3-10 ys)= (19.6 X weight in kg)+ (1.033 X height in cm)+414.9
  - » Girls (10-18 ys)= (8.365 X weight in kg)+ (4.65 X height in cm)+200
  - » Boys (10-18 ys)=(16.25 X weight in kg)+ (1.372 X height in cm)+515.5

Protein Requirement:

- 1.5-2 g/kg/day

Micronutrients

- Copper: 4-5 mg/day
- Selenium: 300-500 ug/day
- Zinc: 25-40 mg/day
- Vitamin C: 1-3 g/day
- Vitamin A: 10000 IU/day
- Vitamin E: 20-25 IU/day
- Glutamine: 0.3-0.5 g/kg/day

Reduction of metabolism

- Propranolol may be used to decrease hypermetabolism and reduce energy expenditure
  - » Adults: 20 mg/8 hours
  - » Pediatric: 0.5-1 mg/kg every 8 hours
- Dose is adjusted to decrease heart rate by 15-20%

Pain management:

Pain assessment

Pain assessment in adults

- Patient is able to communicate: The Burn Specific Pain Anxiety Scale (BSPAS)
- Patient is not able to communicate: Critical Care Pain Observation Tool (CPOT)

Paint assessment in pediatric

- Non-verbal and preverbal children: Face, Leg, Activity, Cry, and Consolability (FLACC) scale
- Children 4-12 years: Pediatric Pain Assessment Tool (PAAT)

Pain types and management

- Pain management protocol is described in Table 60-3

Background Pain:

- Mild to moderate potent analgesic:
- IV opioid infusion(PCA)
- Oral administration of long acting opioid
- Oral administration on regular schedule of short acting opioid

Procedural Pain:

- Anxiety developed with repeated performance of wound care.
- Potent sedation, analgesia and anxiolytics

Breakthrough Pain:

- Development of opioid tolerance
- Inadequate background analgesic management
- Increase dose or add new analgesics

Chronic pain:

- Lasts longer than 6 months after all burn wounds healed.
- The most common form is neuropathic pain

Table 60-3: Adult and pediatric drug dosing in burn pain management

	No oral intake		Oral intake	
	Adult	Pediatric	Adult	Pediatric
Background pain	Paracetamol AND NSAID+weak opioid agonist (Tramadol or Codeine) OR strong opioid (morphine or Naluphine) if weak opioid is insufficient			
	Paracetamol dose			
	1 gmevery 6 hrs	10 to 15 mg/kg every 6 hours	500 mg p.o. every 6	10 to 15 mg/kg every 6 hours
	NSAID			
	• Diclofenac 75 mg IV every 12 hours in adults, • Ketolac15-30 mg IV/IM every 6 hrs	• Ketolac0.5-1 mg/kg IM/IV every 6 hrs maximum 15-30 mg/6 hrs	• Ibuprofen400 mg Per Os (PO) every 8 hours, or • Diclofenac 50 mgPO every 12 hours	• Ibuprofen10 mg/kg every 8 hours in children over 6 months of age • Diclofenad to 2 mg/kg every 12 hours in children over 5 years of age

	Weak opioid (Tramadol or codeine)			
	• 50 to 100 mg Intravenous (IV) every 6 to 8 hours maximum 400 mg/day • Codeine30 to 60 mg PO every 6 hours in adults, maximum 240 mg/day	• Tramadol 1mg/kg/dose every 6 to 8 hours • Codeine 1mg/kg/dose every 6 to 8 hours	• Tramadol 50 to 100 mg Intravenous (IV) every 6 to 8 hours maximum 400 mg/day	• Tramadol 1 mg/kg/dose every 6 to 8 hours
	Strong Opioid (Morphine or Naluphine)			
	Morphine 15–30 mg/4 hrs	Morphine 0.3 mg/kg/4 hrs	Morphine 2–10 mg every Naluphine 10–20 mg every 6 hrs	0.1 mg/kg/4 hrs Naluphine 0.4 mg/kg/every 6 hrs Ketamine IV
Procedural pain			• ketamine IV 0.5–1.0 mg/kgIM 4–5 mg/kg • Propofol IV 0.5–1.0 mg/kg Additional dose 0.5 mg/kg • Ketamine + propofol Mixture ofketamine to propofol ratio 1:3 (30 mg ketamine+90 mg propofol in 20 ml Syringe) Dose: 0.05 ml/kg followed by 0.25 ml/kg for the subsequent dose • Fentanyl.0.5–1 pg/kg • Dexmedetomidine • 1.0 pg/kg loading followed by 0.2–0.7 pg/kg/hr	• Ketamine IV 1.0–2.0 mg/kg/15–20 min IM 4–5 mg/kg • Propofol IV 1.0 mg/kg. additional dose 0.5 mg/kg • Ketamine+ propofol Mixture of ketamine to propofol ratio 1:3 (30 mg ketamine+90 mg propofol in 20 ml Syringe) Dose: 0.05 ml/kg followed by 0.25 ml/kg for the subsequent dose • Fentanyl1–2 pg/kg • Dexmedetomidine 1.0 pg/kg loading followed by 0.5–2.0 pg/kg/hr

Chronic pain			• Gabapentin 300 mg every 8 hrs Max 3600 mg/ day • Pregabalin 150-600 mg/day in 2-3 divided doses	• Gabapentin 10 mg/kg day • Pregabalin > 30 kg 2.5-10 mg/kg in 2-3 divided doses <30 kg 3.5-14 mg/kg in 2-3 divided doses

Sepsis management:

- Surviving Sepsis After Burn Campaign (SSABC) is an updated sepsis management of burn patient developed by international group of burn experts to improve burn sepsis outcomes.

Triggers for considering the diagnosis of sepsis in burn patients

- Change in SOFA ≥2 points
- Lactate change > 2 mmol/L (> 18 mg/dl) (a base deficit surrogate)
- Temperature change - new fever or hypothermia (no consensus on threshold temperature)
- Acute drop in platelet count
- Urine output drop/increased fluid requirements
- Kidney Disease Improving Global Outcomes (KDIGO) Acute Kidney Injury Stage ≥1
- Respiratory changes
- Alterations of mental status
- Gastrointestinal dysfunction
- Change in wound appearance suggestive of infection
- Procalcitonin increase ≥ 2 ng/ml from initial level

Prevention of Sepsis

- Barrier precautions should be used to prevent infection in major burns.
- The routine use of methicillin-resistant Staphylococcus aureus (MRSA) screening is not clear and will depend on the baseline rate of MRSA in the individual burn unit.
- Wound cultures should be obtained, where possible, prior to initiation of antibiotics if the signs or symptoms of infection are present.
- Burn wounds should be washed with running water (shower or trolley hydrotherapy) for each dressing change.
- Burn wounds should be washed at least daily when there are concerns for infection.
- Sterile water is not necessary to wash the wounds. Potable tap water is usually adequate. The decision to use water to cleanse wounds should consider the quality of water.
- Ventilator-associated Pneumonia (VAP) bundles should be used to reduce the risk for pneumonia in burn patients.
- There was no consensus regarding the practice of scheduled central line changes to reduce central line-associated blood stream infections (CLABSIs).

- Selective gut decontamination should not be used to reduce infections.
- Topical antimicrobial ointments or dressings should be used to reduce burn-related sepsis until wound excision and coverage is accomplished.
- Prophylactic systemic antibiotics should not be used to prevent burn-related sepsis.
- Prophylactic systemic antibiotics do not prevent sepsis in burn patients, and they may select resistant organisms.

Diagnostic Tests and Screening

- Blood cultures should be collected whenever possible prior to initiating antibiotics.
- Urine and sputum cultures are less time-critical but recommended as long as they do not delay delivery of antibiotics. Endotracheal aspirates, bronchoalveolar lavage or protected distal sampling are preferred for sputum cultures.
- Superficial swab wound cultures should be obtained if there is a change in the appearance in the wound. Deep tissue cultures are not necessary.
- All laboratory tests should be interpreted in the context of trends, not just on a single laboratory finding.
- An elevated white blood count (WBC) is poorly indicative of sepsis in burns.
- Procalcitonin may be considered for the diagnosis of sepsis but not in isolation.

Treatment of sepsis

Antimicrobial therapy

- Empiric broad spectrum antibiotics should be started within 1 hour for septic shock and 3 hours for sepsis.
- The choice of antibiotics should be based on regional and unit-specific antibiograms (local prevalence of resistance) and recent patient-specific cultures.
- Antifungal therapy should not routinely be added to empiric broad spectrum antibiotics for patients with sepsis or septic shock.
- In patients with burn sepsis or septic shock, antifungal therapy should be considered if patient has significant risk factors, such as:
    - Recently treated with a long course of broad spectrum antibiotics
    - Documented colonization, recently treated fungal infection, or has a wound visually concerning for possible fungus
    - Prolonged use of exogenous systemic steroids or intravenous lipids (i.e., total parenteral nutrition,or propofol),
    - Recent gastrointestinal complication requiring surgery.
- Antimicrobial therapy should be reassessed daily for possible de-escalation or modification in the patient being treated for sepsis or septic shock.
- Procalcitonin may be used as an adjunct for the decision to stop or de-escalate antibiotics.
- Monotherapy is preferred for the treatment of burn-related sepsis when culture sensitivities are known. (This may change depending on the organism and likelihood to attain optimal pharmacodynamic targets.)
- Shorter duration of antibiotic treatment (i.e., 1 week) is preferred over longer treatment (2 or greater weeks) when the patient is responding, and source control has been addressed.

Source Control

- The burn wound should be examined within one hour of diagnosis and if there are signs of invasive infection, the wound should be excised as soon as feasible.
- Tissue specimens of suspected infected wounds should be sent for culture to guide antibiotic therapy.
- For superficial wounds, if there is no "invasive" infection, but cellulitis is present, systemic antibiotics are appropriate.
- Indwelling devices (lines, catheters) that are not essential for active treatment should be removed. In the case of sepsis with no other identified source, strong consideration should be given to removing or replacing existing indwelling catheters.

Hemodynamic management and fluid resuscitation

- Fluid resuscitation and hemodynamic management are the same as in non-burn septic shock patients

Toxic Shock Syndrome:

Recognition

- It is a diagnosis that is often missed because of non-specific signs
- Abbreviated criteria for diagnosis of toxic shock syndrome in children
  - » Pyrexia
  - » Rash
  - » Diarrhea
  - » Irritability, confusion
  - » Hypotension, tachycardia
  - » Lymphopenia

Resuscitation

- The same as septic shock
- Removal of the source of infection
  - » Surgical debridement of wounds, drainage of abscesses
- Rational choice of antibiotics
  - » Consider adding vancomycin or teicoplanin
- Adjunctive therapy
  - » Clindamycin: 20-40 mg/kg/day in 2 to 3 divided doses
  - » Intravenous immunoglobulin: 400-500 mg/kg once OR
  - » FFP 10 ml/kg if immunoglobulin is not available

Specific types of burn

Inhalational burn

- Inhalational injury is non-specific term which refers to damage to respiratory tract or lung tissue from heat, smoke, or irritant carried into airway during inspiration

Diagnosis

- Assessment of carboxyhemoglobin concentration by using arterial blood gases for CO-oximetric measurement or using pulse oximeter capable with multi wave length e.g. Masimo SPO2
- CT chest and assessment of bronchial wall thickness (BWT). BWT was measured 2 cm distal from the tracheal bifurcation . BWT> 3 mm predicts pneumonia (Figure 60-4)

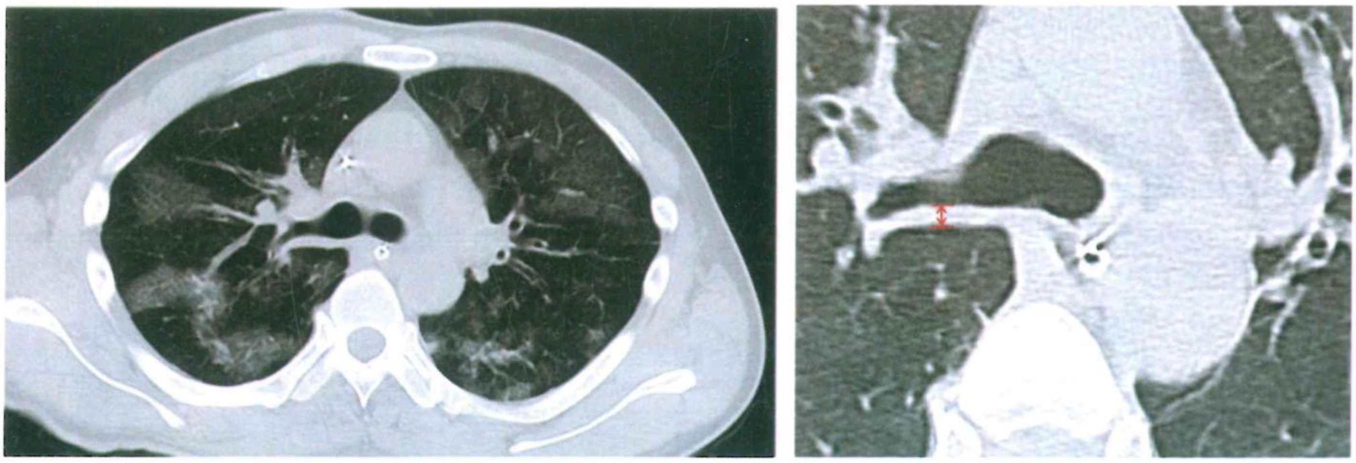


Figure 60-4: Assessment of bronchial wall thickness

Management:

- All patients should receive 100% oxygen by face mask to displace carbon monoxide
- Securing airway: Patient will need intubation if he has any of the following signs
  - » Stridor
  - » Use accessory muscle of respiration
  - » Deep burn to face or neck
  - » Edema of the oropharynx
- In all intubated patients, FIO2 should be placed on 100% until clearance of carbon monoxide
- Extubation criteria
  - » In additional to standard extubation criteria, leak test should be positive.
- Hyperbaric oxygen might be considered in
  - » CO level > 25 percent (> 20 percent if pregnant)
  - » Loss of consciousness
  - » Severe metabolic acidosis (pH < 7.1)
  - » Concern for end-organ ischemia (chest pain, ECG changes, altered mental status)
- Pneumonia care
  - » Bronchodilators if patient develop bronchospasm or wheezes
  - » Inhaled N Acetylcysteine: 3ml 20% solution every 4 hours
  - » Inhaled Heparin: 5000 units in 3 ml saline every 4 hours

References:

1. Greenhalgh DG, Hill DM, Burmeister DM, et al Surviving Sepsis After Burn Campaign. Burns. 2023 6:S0305-4179:00089-X
2. McGovern C, Puxty K, Paton L. Major burns: part 2. Anaesthesia, intensive care and pain management. BJA Educ. 2022;22:138-145
3. Zhang P, Zou B, Liou YC, Huang C. The pathogenesis and diagnosis of sepsis post burn injury. Burns Trauma. 2021 4;9:tkaa047
4. Causbie, J.M.; Sattler, L.A.; Basel, A.P.; Britton, G.W.; Cancio, L.C. State of the Art: An Update on Adult Burn Resuscitation. Eur. Burn J. 2021, 2, 152-167
5. Bittner EA, Shank E, Woodson L, Martyn JA. Acute and perioperative care of the burn-injured patient. Anesthesiology. 2015;122:448-64.

SECTION 14

Pain Sedation, and Delirium

Chapter 61

Pain, Agitation, and Delirium

Pain in critically ill patients

General Principle

- Critically ill adults experience moderate-to-severe pain at rest and during standard care procedures
- Clinically significant pain and anxiety have been reported in up to 70 % of ICU patients

Risk factors of pain in ICU

- Postoperative pain
- Procedural pain: The following procedures are associated with the greatest increased pain intensity
    - Arterial line insertion
    - Peripheral IV insertion
    - Central line insertion
    - Peripheral blood draw
    - Femoral sheet removal
    - Respiratory exercises
    - Mouth care
    - Eye care
    - Mobilization
    - Nasogastric tube insertion
    - Nursing care (bathing, sheet-change, repositioning)
    - Extubation.

Pain assessment

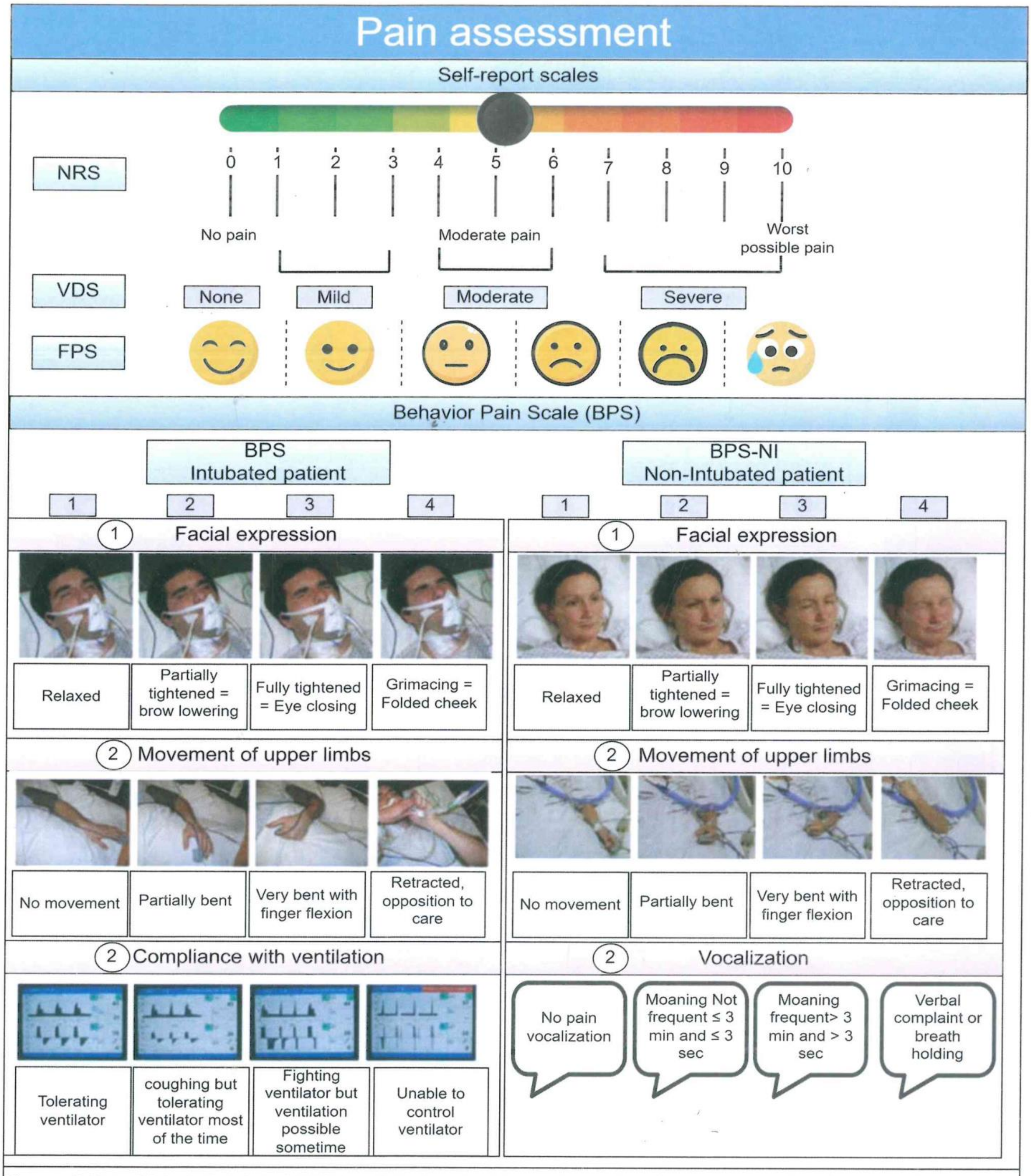
- Management of pain for adult ICU patients should be guided by routine pain assessment.
- Pain assessment monitoring depends on whether the patient is able to self-report pain severity or not.
- Pain monitoring algorithm is described in Figure 61-2

Self-report scale

- In awake patient: pain assessment could be assessed using Numerical Rating Scale (NRS), faces pain scale (FPS), verbal descriptor scale (VDS). (Figure 61-1)

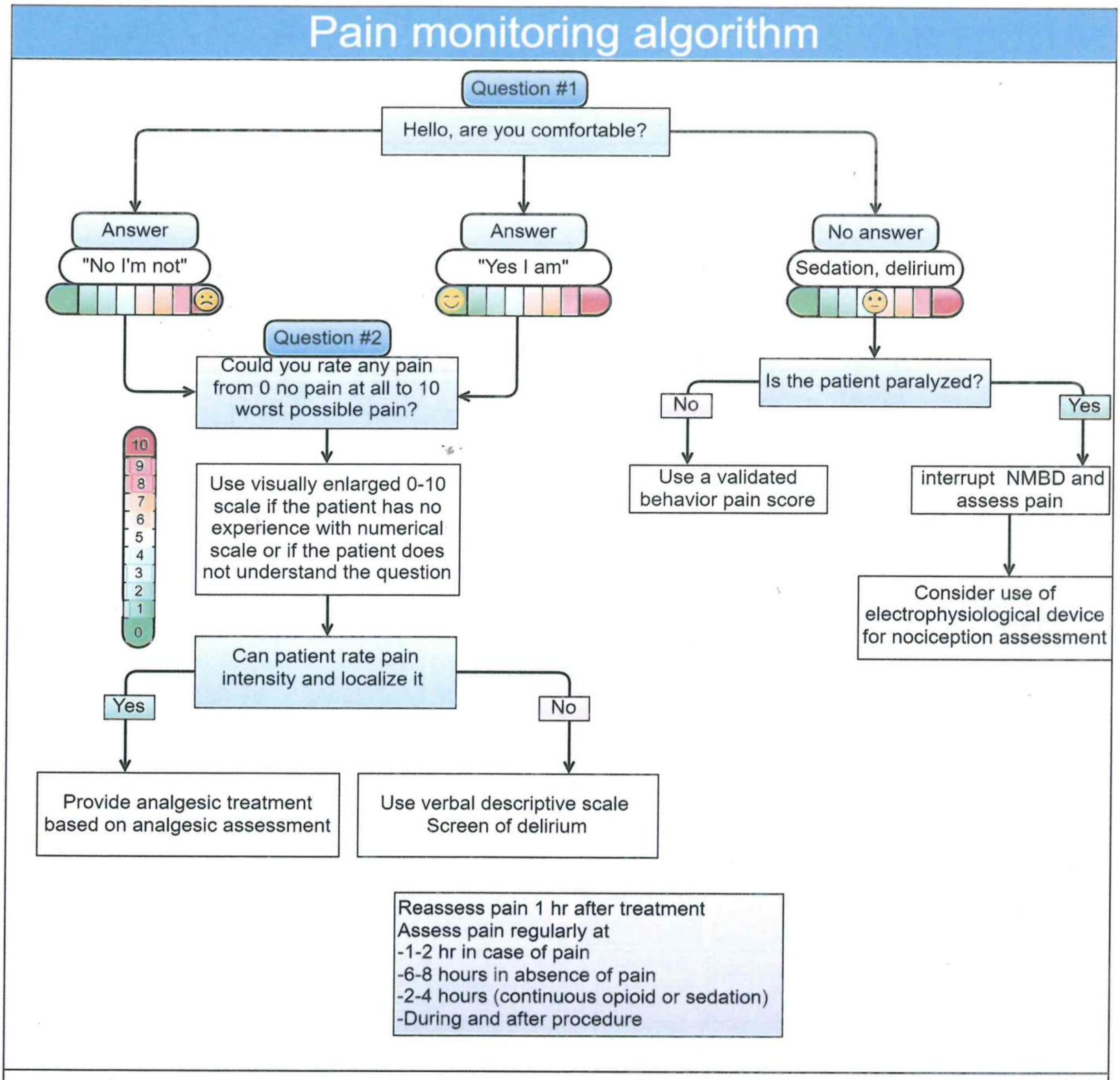
Behavior assessment tool

- In sedated or mechanically ventilated patient: Pain assessment could be done using Behavior Pain Scale (BPS), and nonintubated (BPS-NI) patients and the Critical-Care Pain Observation Tool (CPOT). (Figure 61-1)
- Vital signs (or observational pain scales that include vital signs) should not be used alone for pain assessment in adult ICU patients.


Pain assessment
Self-report scales
NRS
0
1
2
3
4
5
6
7
8
9
10
No pain
Moderate pain
Worst possible pain
VDS
None
Mild
Moderate
Severe
FPS
Behavior Pain Scale (BPS)
BPS Intubated patient
1
2
3
4
① Facial expression
Relaxed
Partially tightened = brow lowering
Fully tightened = Eye closing
Grimacing = Folded cheek
② Movement of upper limbs
No movement
Partially bent
Very bent with finger flexion
Retracted, opposition to care
② Compliance with ventilation
Tolerating ventilator
coughing but tolerating ventilator most of the time
Fighting ventilator but ventilation possible sometime
Unable to control ventilator
BPS-NI Non-Intubated patient
1
2
3
4
① Facial expression
Relaxed
Partially tightened = brow lowering
Fully tightened = Eye closing
Grimacing = Folded cheek
② Movement of upper limbs
No movement
Partially bent
Very bent with finger flexion
Retracted, opposition to care
② Vocalization
No pain vocalization
Moaning Not frequent ≤ 3 min and ≤ 3 sec
Moaning frequent> 3 min and > 3 sec
Verbal complaint or breath holding

Chanques G, Payen JF, Mercier G, de Lattre S, Viel E, Jung B, Cissé M, Lefrant JY, Jaber S. Assessing pain in non-intubated critically ill patients unable to self report: an adaptation of the Behavioral Pain Scale. Intensive Care Med. 2009 ;35:2060-7
NRS: Numeric Rating Scale, VDS: Verbal Descriptor Scale, FPS: Faces Pain Scale, BPS: behavior pain scale NI: non-intubated

Figure 61-1:Pain assessment scales


Pain monitoring algorithm
Question #1
Hello, are you comfortable?
Answer
"No I'm not"
Answer
"Yes I am"
No answer
Sedation, delirium
Question #2
Could you rate any pain from 0 no pain at all to 10 worst possible pain?
10
9
8
7
6
5
4
3
2
1
0
Use visually enlarged 0-10 scale if the patient has no experience with numerical scale or if the patient does not understand the question
Can patient rate pain intensity and localize it
Yes
No
Provide analgesic treatment based on analgesic assessment
Use verbal descriptive scale Screen of delirium
Is the patient paralyzed?
No
Yes
Use a validated behavior pain score
interrupt NMBD and assess pain
Consider use of electrophysiological device for nociception assessment
Reassess pain 1 hr after treatment
Assess pain regularly at
-1-2 hr in case of pain
-6-8 hours in absence of pain
-2-4 hours (continuous opioid or sedation)
-During and after procedure

Chanques G, Gélinas C. Monitoring pain in the intensive care unit (ICU). Intensive Care Med. 2022;48:1508-1511

Figure 61-2: Pain monitoring algorithm

Pain management

Opioid analgesia

- Opioid is the drug of choice for pain management in critically ill patients.
- Either continuous IV infusion or an intermittent scheduled-administration strategy of analgesics is more useful for retaining consistent analgesic action than administration upon patient demand.
- A patient-controlled analgesia (PCA) device helps administer opioids to patients who can understand and handle the device.

- Fentanyl or remifentanil for rapid pain management is useful for patients with acute conditions.
- Fentanyl, hydromorphone, or remifentanil is useful for patients with hemodynamic instability or renal failure.
- Doses and pharmacokinetics of opioid is described in Table 61-1

Non-opioid analgesia

- Acetaminophen, nefopam, ketamine, lidocaine, neuropathic agents could be used as adjuncts to opioid analgesia in critically ill patients
- Nonsteroidal anti-inflammatory drugs (NSAIDs) may be associated with renal toxicity and/or surgical wound bleeding and should NOT be used routinely in critically ill patients.
- Doses and pharmacokinetics of non-opioid are described in Table 61-2

Table 61-1: Dose and pharmacokinetics of opioids

Drug	Time of onset (min)	Elimination half-life (hour)	Accumulation	Dose	
				Intermittent dose	Infusion rate
Fentanyl	1-2	2-4	Kidney and liver dysfunction	30-50 ug q 0.5-1 hr	0.7-10 ug/kg/min
Morphine	5-10	2-4	Liver dysfunction	2-4 mg q 1-2 hr	2-10 mg/hr
Hydromorphone	5-10	2-3	Kidney and liver dysfunction	0.2-0.6 mg q 1-2 hr	0.5-3 mg/hr
Meperidine	5-10	2-4	Liver and kidney dysfunction	12.5-50 mg	NA
Remifentanil	1-2	3-10 (min)	No	Loading 1 ug/kg	0.25-1 ug/kg/min

Table 61-2: Doses and pharmacokinetics of non-opioid analgesic

Drug	Elimination half-life	Elimination half-life (hour)	Accumulation
Acetaminophen (IV)	2	650 mg IV every 4 hr–1,000 mg IV every 6 hr; max dose ≤4 g/day	High dose induces hepatic dysfunction
Ketamine (IV)	2-3	Loading dose: 0.1–0.5 mg/kg IV followed by 0.05-0.4 mg/kg/hr	Hallucinations, other psychological disturbances
Ketorolac	2-8	30 mg IM/IV, then 15–30 mg IM/IV every 6 hr up to 5 day; max dose: 120 mg/day ×5 days	Renal toxicity, GI bleeding
Ibuprofen (IV)	2-3	400–800 mg IV every 6 hr infused over >30 min; max dose: 3.2 g/day	Renal toxicity, GI bleeding

Gabapentin (PO)	5-7	Starting dose: 100 mg PO three times daily; maintenance dose: 900–3,600 mg/day in three divided doses	Sedation, confusion, dizziness, ataxia; adjust dosing in renal failure patients
Carbamazepine (PO)	12-17	Starting dose: 50–100 mg PO bid; maintenance dose: 100–200 mg every 4–6 hr; max dose: 1,200 mg/day	Nystagmus, diplopia, dizziness, lethargy, lightheadedness

Systemic regimen of multimodal intravenous analgesia

- Paracetamol 0.5–1.0 g, intravenous, every 6 h combined (or otherwise) with ketoprofen (50–100 mg), an intravenous infusion every 12 h
- A continuous infusion of an opioid (e.g., morphine, fentanyl, sufentanil, nalbuphine) in a dose determined by titration:
    - » morphine, a single intravenous bolus 2.5–10 mg; the dose can be repeated after 4–6 h or a continuous infusion 0.8–2.5 mg/h or PCA, bolus dose 0.5–2.5 mg, lockout interval 5–15 min, OR
    - » fentanyl, single bolus 50–200 μg; a dose of 50 μg can be repeated after 20–40 min or a continuous infusion, 0.05–0.08 μg/kg/min or PCA, bolus dose 20–50 μg, lockout interval 5–10 min, OR
    - » Nalbuphine, a single intravenous bolus 0.1–0.3 mg/kg (max. 20 mg); the dose can be repeated after 3–6 h or a continuous infusion 0.04–0.32 mg/kg/ h or PCA, bolus dose 1–3 mg, lockout interval 6–10 min

Epidural analgesia regimen for thoracic and abdominal operations

- Epidural analgesia regimen for thoracic, upper, and lower abdominal operations is described in Table 61-3

Procedures Place of epidural catheter implantation	Continuous infusion into the epidural space	Initial dose	Continuous infusion
Thoracic and epigastric surgery T 4-T 8	bupivacaine 0.125% OR ropivacaine 0.2% + combined with fentanyl, (2–5 μg/mL) or sufentanil (0.5–1 μg/ mL)	0.5 mL per segment Titration 5 mL every 10 min	4–8 mL h /hr
Upper abdominal surgery T8-T10	bupivacaine 0.125% OR ropivacaine 0.2% combined with fentanyl, (2–5 μg/mL) or sufentanil (0.5–1 μg/ mL)	1–2 mL per segment Titration 5 mL every 10 min	4–8 mL h /hr
Lower abdominal, pelvic , and lower limb surgery	bupivacaine 0.125% OR ropivacaine 0.2% combined with fentanyl, (2–5 μg/mL) or sufentanil (0.5–1 μg/ mL) or morphine, bolus 2–4 mg, (0.05 mg/mL)	1–2 mL per segment Titration 5 mL every 10 min	8-15 ml/hr

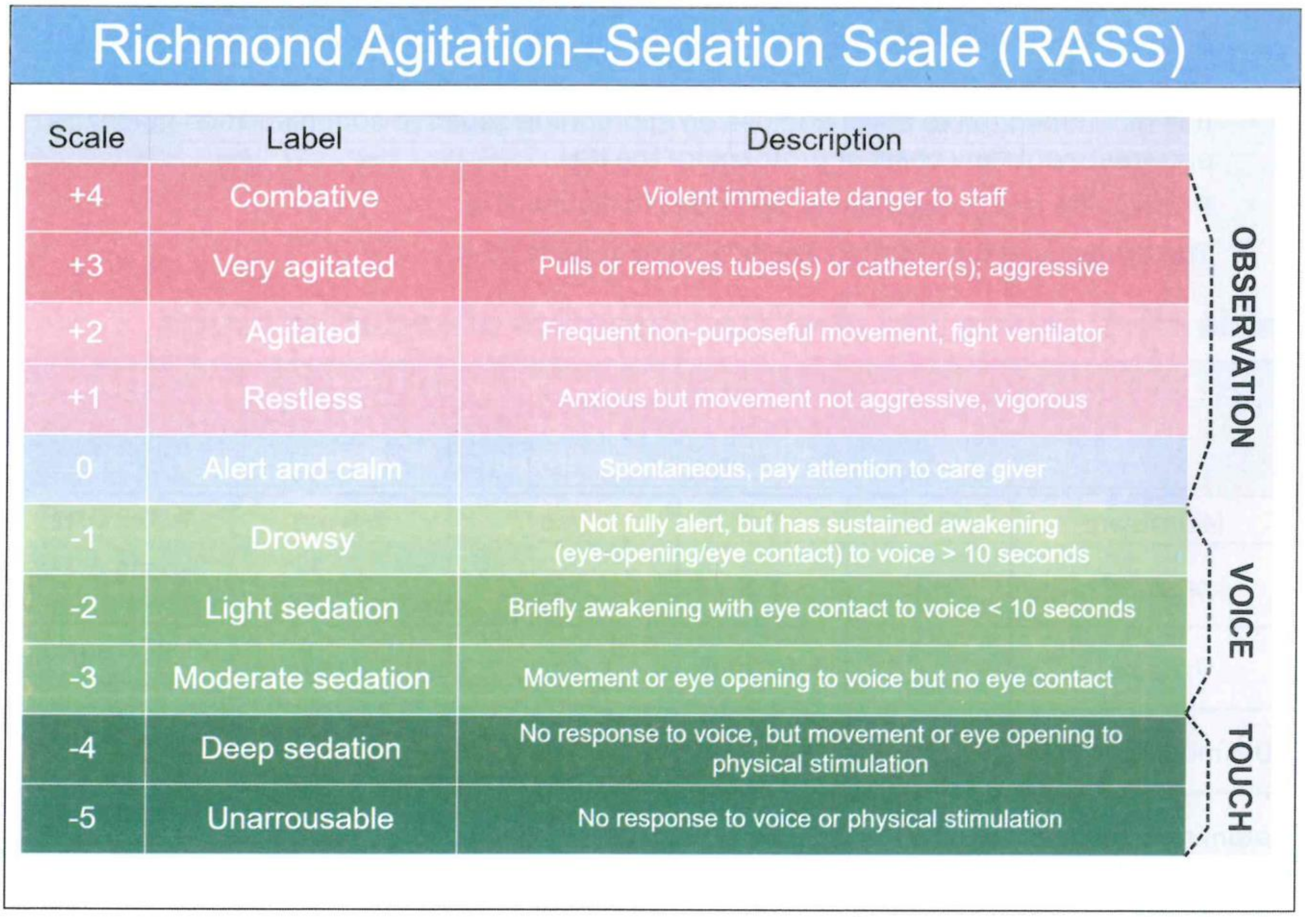
Sedation management of critically ill patients

General principles

- Pain should be treated before a sedative agent is considered. Analgosedation is defined as either analgesia-first sedation (i.e., an analgesic [usually an opioid] is used before a sedative to reach the sedative goal) or analgesia-based sedation (i.e., an analgesic [usually an opioid] is used instead of a sedative to reach the sedative goal).

Sedation assessment

- After adequate pain control, the degree of patient comfort should be assessed using Richmond agitation sedation scale.
- Sedation monitoring based on the bispectral index rather than a subjective scale may facilitate titration of sedation when a sedation assessment scale cannot be used due to deep sleep or muscle relaxants
- Targeted sedation: set goal level of sedation using RASS score and titrate sedation to maintain target
- RASS score is described in (Figure 61-3)



Richmond Agitation–Sedation Scale (RASS)

Scale	Label	Description	
+4	Combative	Violent immediate danger to staff	OBSERVATION
+3	Very agitated	Pulls or removes tubes(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fight ventilator	
+1	Restless	Anxious but movement not aggressive, vigorous	
0	Alert and calm	Spontaneous, pay attention to care giver	
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice > 10 seconds	VOICE
-2	Light sedation	Briefly awakening with eye contact to voice < 10 seconds	
-3	Moderate sedation	Movement or eye opening to voice but no eye contact	
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	TOUCH
-5	Unarrousable	No response to voice or physical stimulation	

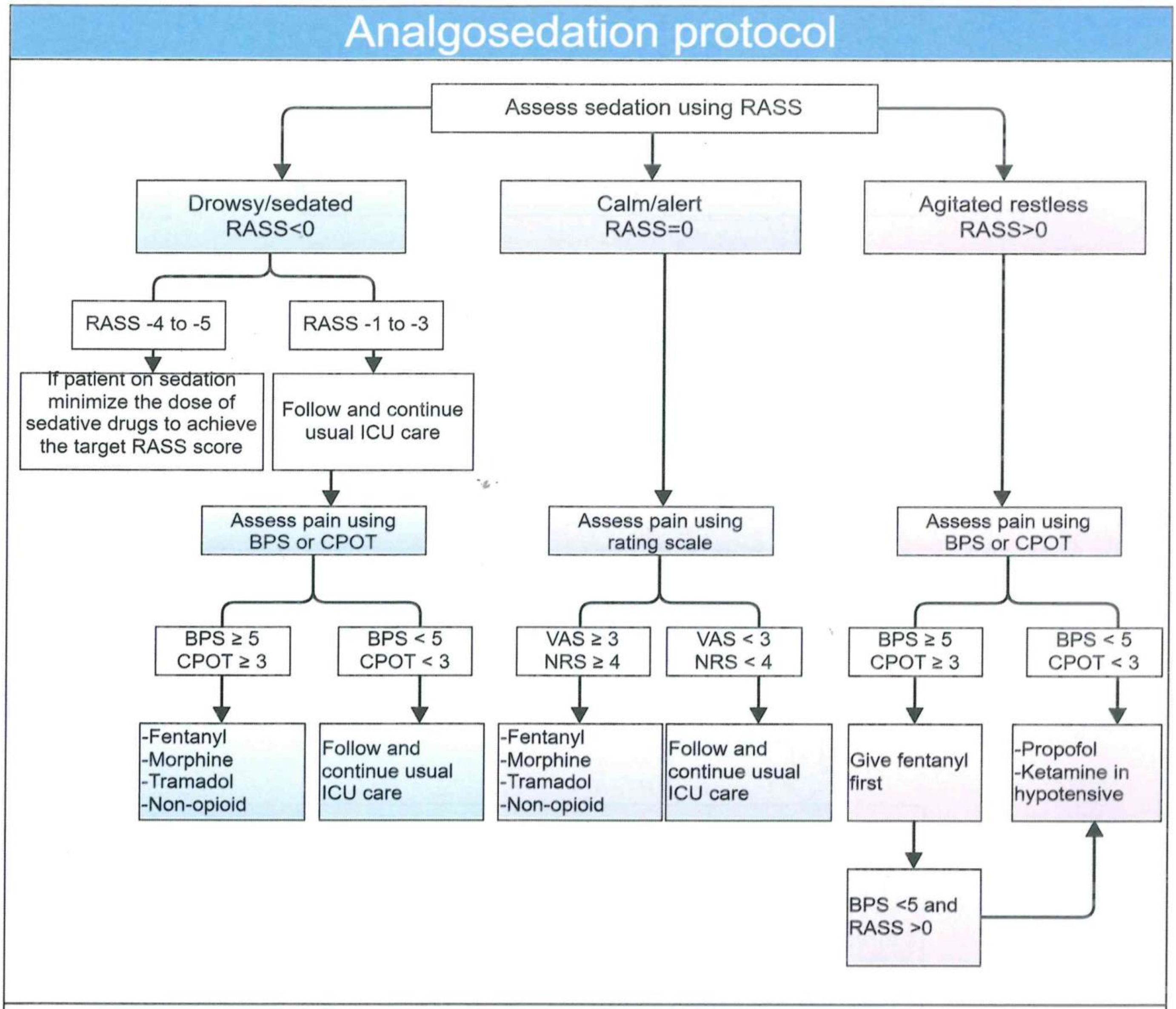
Figure 61-3: Richmond agitation-sedation scale

Sedation management

- Assess sedation by using RASS score after pain control. If RASS > +1, start sedative drugs
- Propofol is useful in patients requiring rapid and frequent awakening for neurologic evaluations or extubation.
- Midazolam use is recommended for shorter time periods because when it is used for more than 48 to 72 hours, it becomes difficult to predict the recovery time or time for extubation.
- It is recommended to use propofol rather than benzodiazepines as a sedative in post-cardiac surgery adults on mechanical ventilation.
- Propofol and dexmedetomidine are recommended as sedatives rather than benzodiazepines in mechanically ventilated medical and surgical patients not undergoing cardiac surgery. However, benzodiazepines are recommended for alcohol withdrawal syndrome.
- Systematically applied reduction or adjustment of the sedative dose to reach the daily goal of sedation level is recommended to avoid unnecessary long-term sedation.
- Serum triglyceride concentrations should be monitored starting two days after propofol administration, and the fat calories in the emulsion should be included in the total calories.
- It is recommended to make and use an appropriate sedative administration guideline and treatment flow chart or protocol for the ICU.
- Protocol for analgosedation is described in Figure 61-4
- The drugs used for sedation are described in Table 61-4

Table 61-4: Doses and pharmacokinetics of sedative drugs

Drug	Time of onset (min)	Duration (hour)	Accumulation in renal impairment	Dose	
				Bolus	Infusion
Midazolam	2-10	1-4	Yes	2-5 mg	1-20 mg/hr
Lorazepam	5-20	6-8	Yes	2 mg	2-6 mg q 4-6 hr
Propofol	30-50 (sec)	3-10 (min)	No	0.2-2 mg/kg	50-200 ug/kg/min
Dexmedetomidine			No	1 ug/kg over 10 min	0.2-0.7 ug/kg/hr
Ketamine + propofol Mixture of ketamine to propofol ratio 1:3 (30 mg ketamine+90 mg propofol in 20 ml Syringe)				Dose: 0.05 ml/kg	0.25 ml/kg for the subsequent dose


Analgosedation protocol
Assess sedation using RASS
Drowsy/sedated
RASS<0
Calm/alert
RASS=0
Agitated restless
RASS>0
RASS -4 to -5
RASS -1 to -3
If patient on sedation minimize the dose of sedative drugs to achieve the target RASS score
Follow and continue usual ICU care
Assess pain using BPS or CPOT
Assess pain using rating scale
Assess pain using BPS or CPOT
BPS ≥ 5
CPOT ≥ 3
BPS < 5
CPOT < 3
VAS ≥ 3
NRS ≥ 4
VAS < 3
NRS < 4
BPS ≥ 5
CPOT ≥ 3
BPS < 5
CPOT < 3
-Fentanyl
-Morphine
-Tramadol
-Non-opioid
Follow and continue usual ICU care
-Fentanyl
-Morphine
-Tramadol
-Non-opioid
Follow and continue usual ICU care
Give fentanyl first
-Propofol
-Ketamine in hypotensive
BPS <5 and RASS >0

Temesgen N, Chekol B, Tamirie T, Eshetie D, Simeneh N, Feleke A. Adult sedation and analgesia in a resource limited intensive care unit - A Systematic Review and evidence based guideline. Ann Med Surg (Lond). 2021 Apr 30;66:102356.

RASS: Richmond agitation sedation scale, NRS: Numeric Rating Scale, VAS: Verbal Analogue Scale, BPS: behavior pain scale, CPOT: Critically-ill Pain Observation Tool

Figure 61-4: Analgosedation protocol

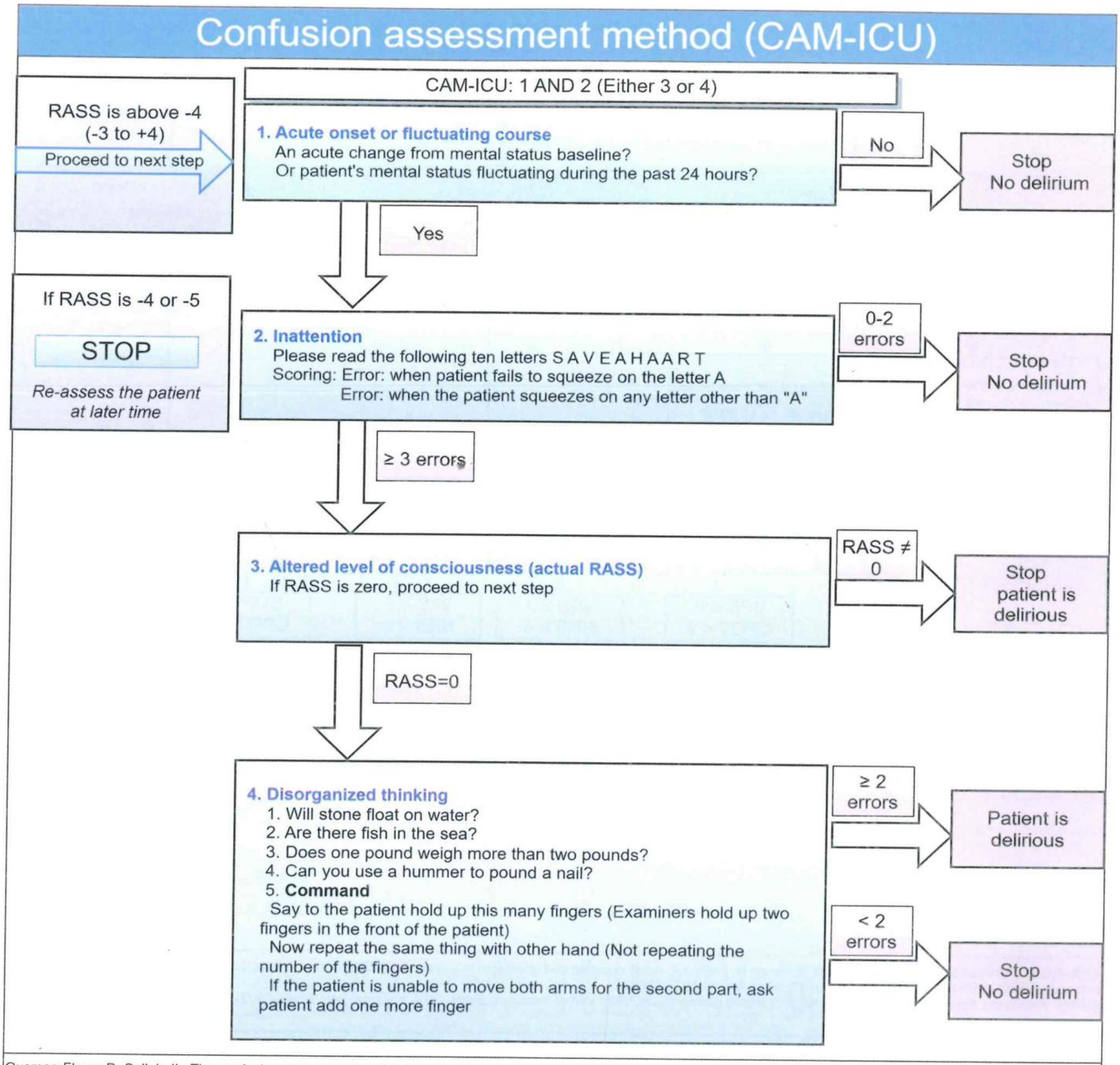
Delirium management of critically ill patients

General principles

- Delirium is defined as a disturbance of consciousness with inattention accompanied by a change in cognition or perceptual disturbance that develops over a short period of time (hours to days) and fluctuates over time

Delirium assessment

- The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are the most valid and reliable delirium monitoring tools recommended for use in adult ICU patients. (Figure 61-5)
- CAM-ICU should be done at least twice daily
- CAM-ICU cannot be done in patient with RASS -4 or-5


Confusion assessment method (CAM-ICU)
CAM-ICU: 1 AND 2 (Either 3 or 4)
RASS is above -4
(-3 to +4)
Proceed to next step
If RASS is -4 or -5
STOP
Re-assess the patient at later time
No
Stop
No delirium
Yes
0-2 errors
Stop
No delirium
≥ 3 errors
RASS ≠ 0
Stop
patient is delirious
RASS=0
≥ 2 errors
Patient is delirious
< 2 errors
Stop
No delirium

1. Acute onset or fluctuating course
An acute change from mental status baseline?
Or patient's mental status fluctuating during the past 24 hours?

2. Inattention
Please read the following ten letters SAVEAHAART
Scoring: Error: when patient fails to squeeze on the letter A
Error: when the patient squeezes on any letter other than "A"

3. Altered level of consciousness (actual RASS)
If RASS is zero, proceed to next step

4. Disorganized thinking
1. Will stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two pounds?
4. Can you use a hummer to pound a nail?
5. **Command**
Say to the patient hold up this many fingers (Examiners hold up two fingers in the front of the patient)
Now repeat the same thing with other hand (Not repeating the number of the fingers)
If the patient is unable to move both arms for the second part, ask patient add one more finger

Gusmao-Flores D, Salluh JI, The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. Crit Care. 2012 3;16(4):R115
RASS: Richmond Agitation–Sedation Scale

Figure 61-5: Confusion assessment method (CAM-ICU)

Delirium management

- Pharmacologic treatment for preventing delirium in critically ill patients is not recommended
- Routine use of haloperidol, an atypical antipsychotic, a statin, or dexmedetomidine is not recommended for delirium treatment. However, treatment of delirium using these drugs can be considered if the symptoms of delirium may be harmful to patients.
- A multicomponent (ABCDEF bundle) nonpharmacologic intervention strategy for the prevention and treatment of delirium is recommended (Figure 61-6)
- Sleep disturbance is a common risk factor for delirium in the ICU. Appropriate control of sleep disturbance can prevent delirium.

- A sleep-promoting protocol (offering earplugs and eye-shades, avoiding unnecessary examinations) should be used to improve the sleep of critically ill patients.
- Drugs for treatment of delirium is described in Table 61-5

Table 61-5: Dose and pharmacokinetic of drugs used in delirium management

Drug	Types of drug	Starting dose	Maximum	Sedation	Extrapyramidal symptoms
Haloperidol	Typical anti-pshychotic	0.5 mg	25 mg	Low	High
Olanzapine	Atypical anti-pshychotic	2.5 mg	20 mg	Moderate	Moderate
Quetiapine	Atypical anti-pshychotic	12.5 - 50 mg	50 mg	High	Very low
Risperidone	Atypical anti-pshychotic	0.5 mg	3 mg	Low	High
Ziprasidone	Atypical anti-pshychotic	5-10	40 mg	Moderate	Moderate

ABCDEF bundle

A — Assess, prevent, & manage pain

-BPS or CPOT to assess pain and ensure adequate pain control
-Analgesia-based sedation with fentanyl
-Use of regional anesthesia and nonopioid adjuncts

B — Both SAT and SBT

-Daily linked SAT and SBT
-Faster liberation from mechanical ventilation
-Multidisciplinary coordination of care

C — Choice of sedation

-Targeted light sedation when sedation is necessary
-Avoidance of benzodiazepine
-Dexmedetomidine if high delirium risk, cardiac surgery, MV weaning

D — Delirium monitoring and manageemnt

-Routine CAM-ICU or ICDSC assessment
-Non-pharmacological intervention include sleep hygiene
-Dexmedetomidine or antipsychotic if hyperactive symptoms

E — Early mobility and exercise

-Physical and occupational therapy assessment
-Coordinate activity with SAT or periods of no sedation
-Progress through range of motion, setting, standing, walking

F — Family engagement and empowerment

-Reorientation, provision of emotional and verbal support
-Cognitive stimulation, participation in mobilization
-Participation in multidisciplinary rounds

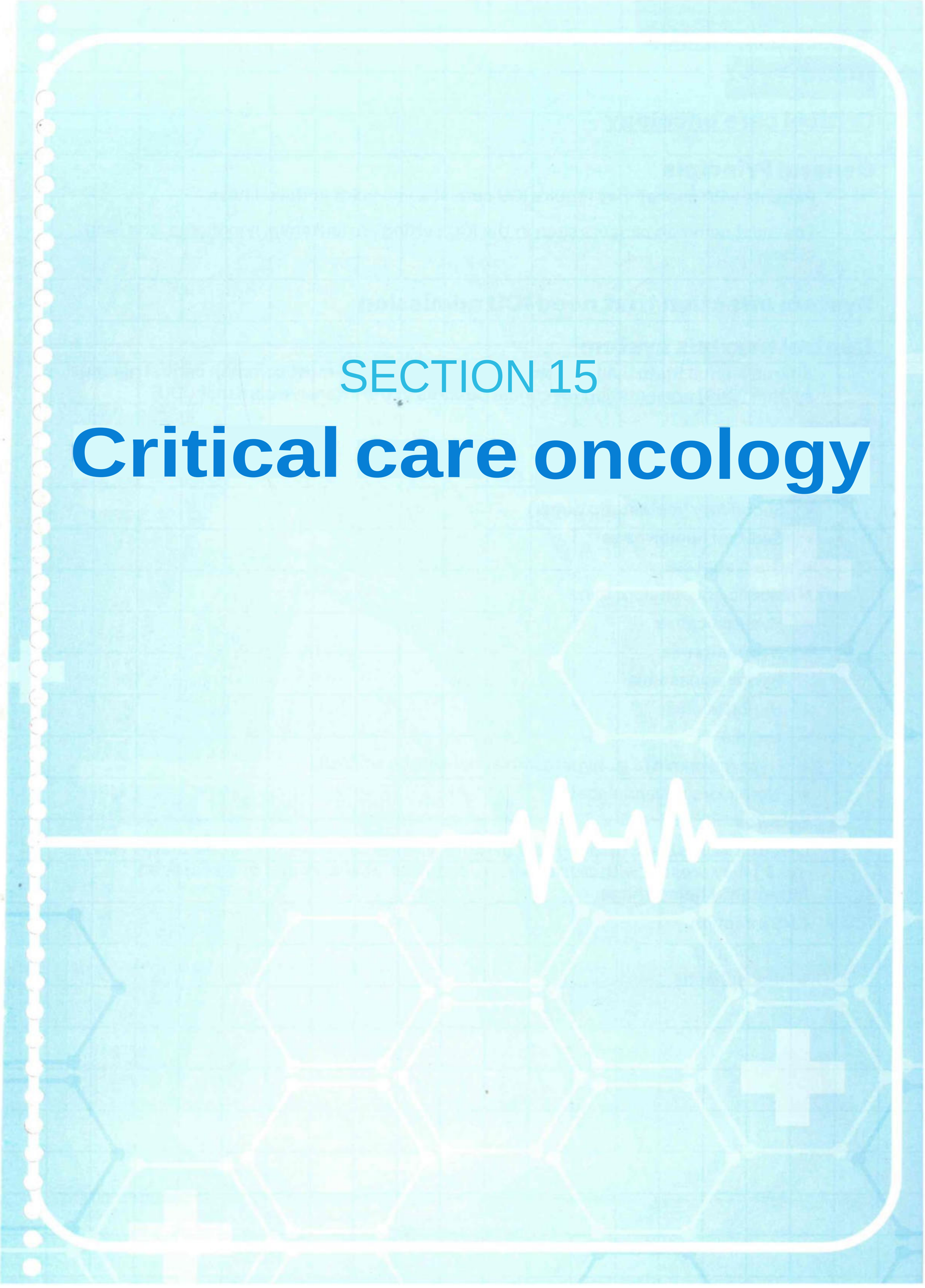
Devlin JW, Skrobik Y, Gélinas C,et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med. 2018;46:e825-e873.

SAT: spontaneous awakening trial, SBT: spontaneous breathing trial BPS: behavior pain scale, CPOT: Critically-Ill Pain Observation Tool

Figure 61-6:ABCDEF bundle

References:

1. Temesgen N, Chekol B, Tamirie T, Eshetie D, Simeneh N, Feleke A. Adult sedation and analgesia in a resource limited intensive care unit – A Systematic Review and evidence based guideline. Ann Med Surg (Lond). 2021 Apr 30;66:102356.
2. Devlin DW, Skrobik Y, Gélinas C,et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med. 2018;46:e825–e873.
3. Seo Y, Lee HO, Ha E0, Ha TS. 2021 KSCCM clinical practice guidelines for pain, agitation, delirium, immobility, and sleep disturbance in the intensive care unit. Acute Crit Care. 2022;37:1–25



SECTION 15

Critical care oncology

SECTION 15

Chapter 62

Critical care oncology

General Principle

- Patients with cancer may require ICU care at some point in their illness.
- The most common cancers seen in the ICU setting are leukemia, lymphoma, and lung cancer

System affection that need ICU admission

Central nervous system

- Altered Mental Status. Alteration in mental status is the most common central nervous system (CNS) presentation for cancer patients in the intensive care unit (ICU)

Causes

- Intracranial mass lesion
  - » Primary tumor of CNS
  - » Secondary (metastatic tumor)
  - » Cerebral hemorrhage
  - » Brain abscess
- Metabolic encephalopathies
  - » Hypercalcemia
  - » Hyponatremia
  - » Hypomagnesemia
  - » Hypoglycemia
  - » Uremia
  - » Hyperglycemia (e.g., hyperosmolar nonketotic acidosis)
  - » Wernicke's encephalopathy
- Seizures
- Cerebral leukostasis: (defined as a peripheral white blood cell [WBC] count >100,000/ mm3) may present with blurred vision, dizziness, ataxia, stupor or coma, or an intracranial hemorrhage
- CNS infection
  - » Meningitis
  - » Encephalitis

Diagnostic modalities

- Arterial blood gases
- Serum electrolytes
- CT/MRI brain
- Lumbar puncture

Management

- Raised intracranial tension
  - » Corticosteroids
  - » Hyperosmolar therapy
  - » Neurosurgical consultation
- Seizures
  - » Correct metabolic alteration or hypoxemia
  - » Anticonvulsant therapy
  - » Metastasis should be treated with corticosteroids, radiotherapy, surgical excision.
- Other modalities
  - » Leukapheresis is one of the therapeutic options for severe symptomatic leukocytosis with leukostasis
  - » Treatment of hydrocephalus

Pulmonary

- » The lungs are involved commonly in cancer patients, with 75-90% of pulmonary complications being secondary to infection.
- » Noninfectious complications include those due to chemotherapy (i.e., bleomycin), thoracic irradiation, and pulmonary resections.
- » Respiratoryfailure in cancer patients requiring mechanical ventilation is associated with a 75% mortality rate.

Causes

- Localized infilterates is suggestive of bacterial infection
- Diffuse bilateral infiltrates are more suggestive of opportunistic infection, treatment-induced lung injury, or lymphangitic spread of carcinoma.
- Bilateral perihilar infiltrates in patients who have rapidly gained weight support a diagnosis of fluid overload.
- Pulmonary infiltrates following bone marrow transplantation
  - » Bacterial pneumonia
  - » Viral CMV pneumonia comprises the majority of interstitial pneumonitides
  - » Bronchiolitis obliterans syndrome as a manifestation of graft versus host disease of the lung.
  - » Pulmonary hypertension.
  - » Diffuse alveolar hemorrhage

- Drug-induced lung injury
  - Large number of chemotherapeutic agents can produce pulmonary toxicity, either actively or delayed years after therapy.
  - Commonly used agents with known pulmonary toxicity include alkylating agents (i.e., cyclophosphamide, carmustine, chlorambucil, melphalan, busulfan), antimetabolites (i.e., methotrexate, azathioprine), antitumor antibiotics (i.e., bleomycin, mitomycin], and alkaloids (i.e., vincristine).
  - Pulmonary toxicity may take the following forms:
  - Noncardiogenic pulmonary edema (ARDS)
  - Chronic pneumonitis and fibrosis
  - Hypersensitivity pneumonitis (i.e., procarbazine, methotrexate, bleomycin)

Diagnosis

- CBC, arterial blood gases
- Sputum culture
- Blood culture
- PCR molecular diagnostics
- CT chest

Management of leukostasis

- Myeloblast counts >50,000/mm 3 warrant prompt treatment for reduction of the total WBC count to 20-60% within hours of recognition of the syndrome.
- Leukapheresis.
- Chemotherapy (i.e., daunorubicin, cytosine arabinoside, hydroxyurea).
- Adequate hydration.
- Urate nephropathy prevention should be initiated with allopurinol and urine alkalinization.
- Hemodynamic monitoring is suggested.
- When ARDS results from leukostasis, the following should be carried out expeditiously:
  - Fluid resuscitation to restore blood volume.
  - Cardiac output and hemodynamics should be optimized through volume enhancement and inotropic agents as needed.
  - Pulmonary vasoconstriction should be treated with a combination of volume expansion, inotropic agents, and supplemental oxygen

Cardiovascular

Cardiac tamponade causes

- Metastatic tumors of the pericardium.
- Primary tumors of the pericardium.
- Postirradiation pericarditis with fibrosis
- Encasement of the heart by the tumor.

Myocardial tissue injury

- Anthracycline antibiotics (i.e., doxorubicin and daunorubicin).
- Mitoxantrone: A total dose >100–140 mg/m2 can cause congestive heart failure and exacerbate preexisting anthracycline-induced cardiomyopathy.
- Cyclophosphamide: Doses >100–120 mg/kg over 2 days can result in congestive heart failure and hemorrhagic myocarditis/pericarditis and necrosis.
- Busulfan: The conventional oral daily dose may cause endocardial fibrosis.
- Interferons: In conventional doses, interferons may exacerbate underlying cardiac disease.
- Mitomycin C: Standard doses can cause myocardial damage.
- Radiation-induced cardiomyopathy causes a dose- dependent endocardial and myocardial fibrosis, which can result in a restrictive cardiomyopathy.

Cardiac Dysrhythmias

- Anthracycline antibiotics cause dysrhythmias unrelated to the cumulative dose; these effects can be seen hours or days after administration.
  - » Commonly observed dysrhythmias include supraventricular tachycardia, complete heart block, and ventricular tachycardia.
- Doxorubicin may also prolong the QT interval.
- Amacrine produces ventricular dysrhythmias.
- Taxol causes bradycardia and in combination with cisplatin may produce ventricular tachycardia

Superior vena cava syndrome

- Ninety-five percent of cases are secondary to extrinsic compression of the SVC by mediastinal malignancy
- The most common tumors are bronchogenic carcinoma of small cell type (48%) and lymphoma (21%)
- Manifestation
  - » Dyspnea aggravated by lying supine or leaning forward.
  - » Tachypnea and signs of airway obstruction.
  - » Signs and symptoms of increased intracranial pressure (i.e., dizziness, headache, visual disturbance, seizure, altered mental status).
  - » Dysphagia, hoarseness.
  - » Neck vein distention, facial plethora, and edema.
  - » Numerous, dilated, vertically oriented, and tortuous cutaneous venules or veins above the rib cage margin.
  - » Upper body edema, with cyanosis and ruddy complexion.
  - » Immediate causes of death are airway obstruction and intracranial hemorrhage. Thrombosis at the SVC may occur in 30% of these patients.

Diagnosis

- ECG, echocardiography

Treatment

- Non-specific treatment. Treat as any case of cardiac tamponade, heart failure or rhythm disturbance.
- Radiation therapy is the mainstay of treatment for most malignant SVC obstruction;

Gastrointestinal

Neutropenic Enterocolitis (Ileocecal Syndrome or Typhlitis)

- Neutropenic enterocolitis commonly occurs in patients with hematologic malignancies (leukemia is the most common, with an incidence of 10-40%) receiving chemotherapy
- Neutropenic enterocolitis results from mucosal ulceration and necrosis of the ileum, cecum, or ascending colon with overgrowth and mural invasion of bacteria and/or fungi
- Clinical Manifestations
  - » Abdominal distention
  - » Right-sided abdominal tenderness
  - » Watery diarrhea
  - » Fever
  - » Thrombocytopenia and neutropenia
- Diagnosis
  - » Clinical suspicion.
  - » Plain radiographs of the abdomen may show ileus with distended cecum and pneumatosis coli.
  - » CT of the abdomen: Thickened bowel wall containing air.
  - » Sigmoidoscopy.
- Treatment
  - » Nutritional support
  - » Nasogastric suction
  - » Broad-spectrum antibiotics with anerobic, gram negative, and Clostridium difficile coverage
  - » Indications for Surgical Exploration
    - Perforation
    - Severe bleeding
    - Abscess
    - Uncontrolled sepsis
    - Failure to improve after 2-3 days of intensive conservative management

Renal and metabolic disorders

Hypercalcemia

- It is the most common metabolic abnormality of cancer patients (10%).
- It may occur with or without bone metastases.
- Causes
  - » Secondary to malignancy 4%
  - » Etiologies other than the malignancy 77%
  - » With coexistent hyperparathyroidism 2%.
  - » Vitamin D intoxication 16%
  - » Idiopathic
- Clinical presentation
  - » Neuromuscular manifestations often predominate and include lethargy, confusion, stupor, and coma (occurs when serum calcium level is >13 mg/dL
  - » Hallucinations and psychosis, weakness, and decreased deep tendon reflexes are also common.

Tumor lysis syndrome

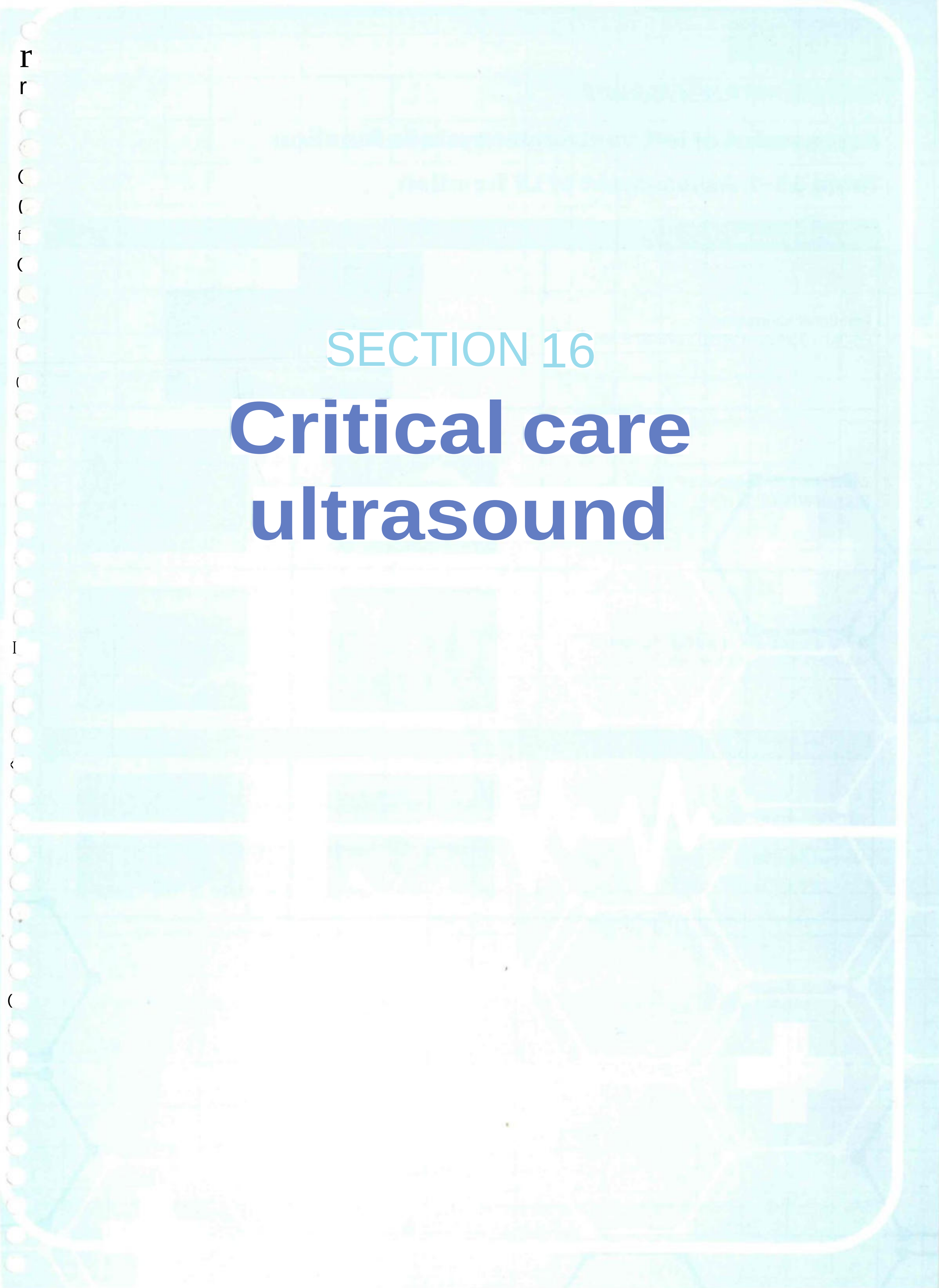
- Tumor lysis syndrome is seen when cytotoxic chemotherapy induces rapid tumor cell lysis in patients with a large malignant cell burden of an exquisitely chemosensitive tumor
- This syndrome classically occurs in patients with Burkitt's and non-Hodgkin's lymphoma, acute lymphoblastic and nonlymphoblastic leukemia, and chronic myelogenous leukemia.
- It may occur spontaneously in patients with lymphomas and leukemias or following treatment with chemotherapy, radiation, glucocorticoids, tamoxifen, and/or interferon
  - » Manifestation
    - Hyperkalemia
    - Hypocalcemia
    - Hyperuricemia
- Management of tumor lysis syndrome
  - » Vigorous IV hydration, often with diuretics or renal-dose dopamine to ensure adequate urine output
  - » Alkalinization of the urine during the first 1–2 days of cytotoxic therapy to increase the solubility of uric acid
  - » Allopurinol to decrease the formation of uric acid
  - » Criteria for hemodialysis in patients unresponsive to the above measures:
    - Serum potassium ≥6 mEq/L
    - Serum uric acid ≥10 mg/dL
    - Serum phosphorus rapidly rising or ≥10 mg/dL
    - Fluid overload

Other Common Metabolic Abnormalities in Cancer Patients

- Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)
  - Occurs in 1–2% of cancer patients
  - Common in small cell carcinoma of the lungs as well as prostatic, pancreatic, ureteral, and bladder carcinomas
- Hypoglycemia
  - Insulinomas: Insulin-secreting, benign, islet cell tumors
  - Non-islet cell tumors (i.e., mesothelioma, fibrosarcoma, hemangiopericytoma, hepatoma, adrenocortical carcinoma, leukemia and lymphoma, pseudomyxoma, pheochromocytoma.

References

1. Martos-Benrtez FD, Soler-Morejon CD, Lara-Ponce KX. Critically ill patients with cancer: A clinical perspective. World *D* Clin Oncol. 2020 24;11:809-835



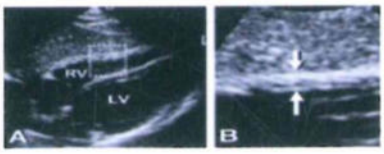
SECTION 16

Critical care ultrasound

Assessment of right ventricle

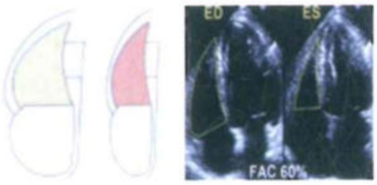
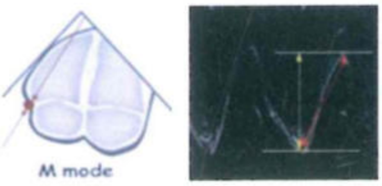
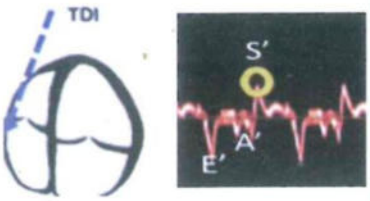
- Assessment of right ventricular size

Table 63-2: Assessment of RV size

Relative Size : » Normal: RV/LV area ratio: ≤0.6 » Dilated: Moderate RV/LV ratio: 0.6- 1.0 » Severe: RV/LV ratio:>1.0	Normal Moderate RV dilatation Severe RV dilatation	» **Standard A4C** » **End diastole** » **Compare RV toLV area**
RV Diameter : » Base: dilated: > 41 mm » Mid cavity dilated: > 35 mm » Base to apex dilated: > 83 mm		» **RV centered A4C** » **End diastole** » **Avoid foreshortening RV** » **Avoid opening up ASC**
RV Wall Thickness : » RV hypertrophy 5mm > Chronic pressure overload pulmonary HTN		» **Subcostal view** » **end diastole** » **2D or M-mode** » **Decrease depth** » **Avoid epicardial fat**

- Assessment of right ventricular function

Table 63-3: Assessment of RV function

Fraction Area Change FAC: » FAC < 35% = RV dysfunction » EDA-ESA/EDA		» **(apex-free wall) during both end diastole and end systole** » **Trace endocardial border** » **Trace beneath trabeculation (Include the trabecula) and TV leaflet**
Tricuspid Annulus Plane Systolic Excursion (TAPSE): » Abnormal if TAPSE < 1.7 cm		» **A4C view Tricuspid lateral annulus excursion measured in M-mode**
Pulsed tissue Doppler S': » Abnormal < 9.5 cm/s		» **view Tricuspid lateral annulus** » **excursion measured in PW TDI**

V

Assessment of pericardium

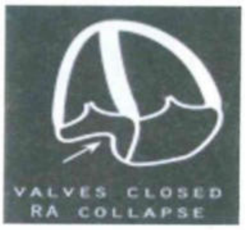
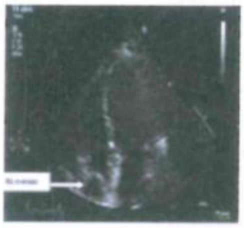
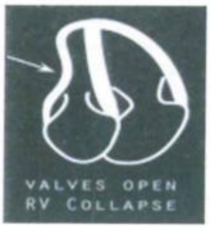
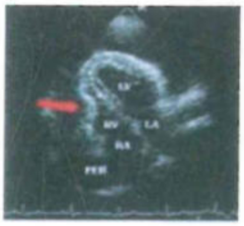
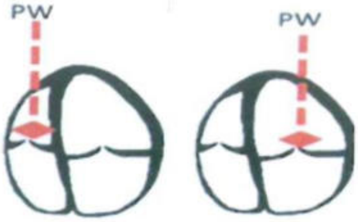
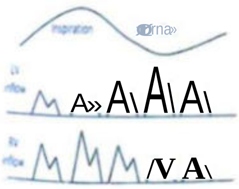
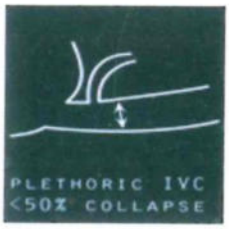
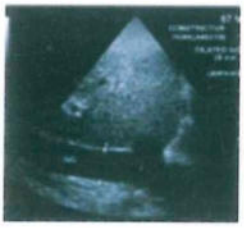
Pericardial effusion

Table 63-4: Severity of pericardial effusion

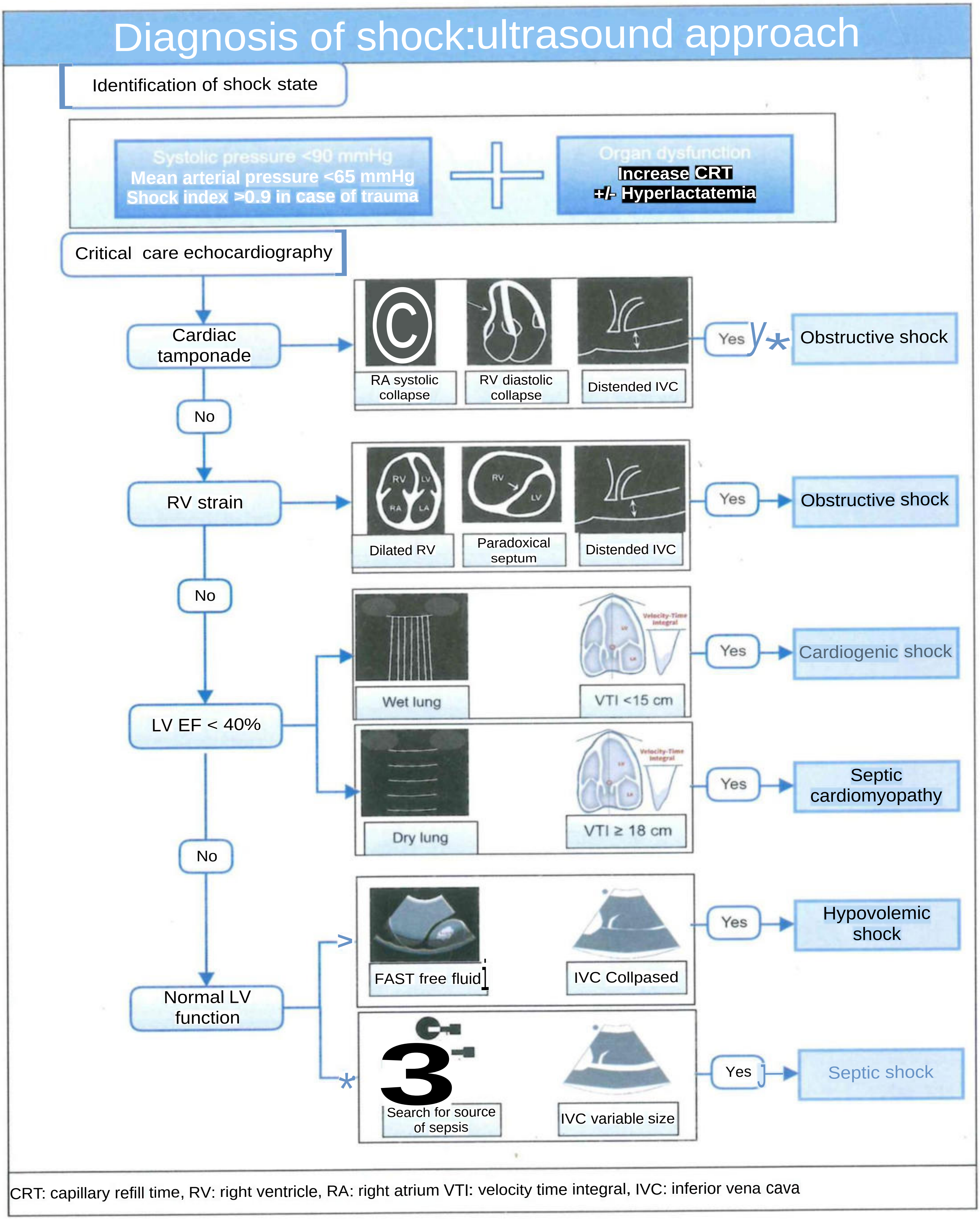
Severity of Pericardial Effusion		
Small	**< 100**	• Clear space detected in systole and diastole posterior only • <1cm in width
Moderate	**100 -** 500 ml	• Clear space detected in systole and diastole anterior and posterior. • 1 - 2 cm
Large	> 500 ml	• Clear space detected in systole and diastole anterior and posterior. • > 2 cm

Pericardial tamponade

Table 63-5: Echocardiographic finding of pericardial tamponade

Right atrium systolic collapse **Best seen in :** » Apical 4 chamber » Subcostal view	 VALVES CLOSED RA COLLAPSE	
Right ventricle diastolic collapse **Best seen in :** » Apical 4 chamber » Parasternal long and short axis view	 VALVES OPEN RV COLLAPSE	
Variation of LVand RV inflow velocity during respiration : » Inspiration-increase RV filling, decrease LV filling » Expiration-decrease RV filling, increase LV filling		 Inspiration LV inflow RV inflow
IVC plethora	 PLETHORIC IVC <50% COLLAPSE	

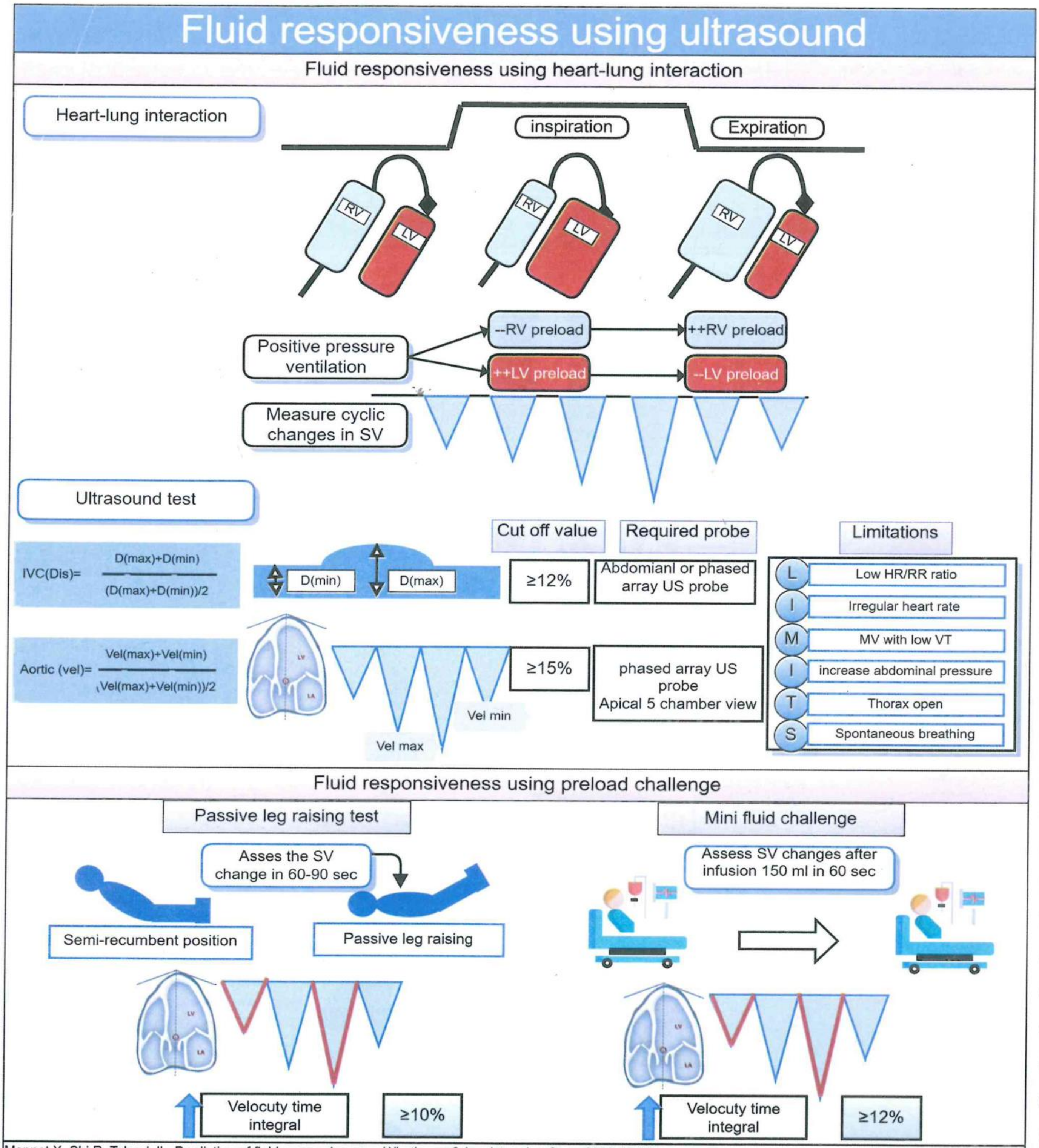
Diagnosis of shock using ultrasound


Diagnosis of shock:ultrasound approach
Identification of shock state
Systolic pressure <90 mmHg
Mean arterial pressure <65 mmHg
Shock index >0.9 in case of trauma
Organ dysfunction
Increase CRT
+/- Hyperlactatemia
Critical care echocardiography
Cardiac tamponade
RA systolic collapse
RV diastolic collapse
Distended IVC
Yes
Obstructive shock
No
RV strain
RV
LV
RA
LA
Dilated RV
Paradoxical septum
Distended IVC
Yes
Obstructive shock
No
LV EF < 40%
Wet lung
VTI <15 cm
Yes
Cardiogenic shock
Dry lung
VTI ≥ 18 cm
Yes
Septic cardiomyopathy
No
Normal LV function
FAST free fluid
IVC Collpased
Yes
Hypovolemic shock
Search for source of sepsis
IVC variable size
Yes
Septic shock

CRT: capillary refill time, RV: right ventricle, RA: right atrium VTI: velocity time integral, IVC: inferior vena cava

Figure 63-1: Diagnosis of shock using ultrasound

Assessment of fluid responsiveness using ultrasound


Fluid responsiveness using ultrasound
Fluid responsiveness using heart-lung interaction
Heart-lung interaction
inspiration
Expiration
RV
LV
Positive pressure ventilation
--RV preload
++LV preload
++RV preload
--LV preload
Measure cyclic changes in SV
Ultrasound test
Cut off value
Required probe
Limitations
IVC(Dis)= D(max)+D(min) / (D(max)+D(min))/2
D(min)
D(max)
≥12%
Abdomianl or phased array US probe
Aortic (vel)= Vel(max)+Vel(min) / Vel(max)+Vel(min))/2
Vel max
Vel min
≥15%
phased array US probe Apical 5 chamber view
L Low HR/RR ratio
I Irregular heart rate
M MV with low VT
I increase abdominal pressure
T Thorax open
S Spontaneous breathing
Fluid responsiveness using preload challenge
Passive leg raising test
Asses the SV change in 60-90 sec
Semi-recumbent position
Passive leg raising
Velocuty time integral
≥10%
Mini fluid challenge
Assess SV changes after infusion 150 ml in 60 sec
Velocuty time integral
≥12%

Monnet X, Shi R, Teboul JL. Prediction of fluid responsiveness. What's new? Ann Intensive Care. 2022;12:46

RV: right ventricle, LV: left ventricle, IVC: inferior vena cava, HR: heart rate, RR: respiratory rate

Figure 63-2: Techniques of fluid responsiveness assessment using ultrasound

Fluid resuscitation guided by inferior vena cava and lung ultrasound

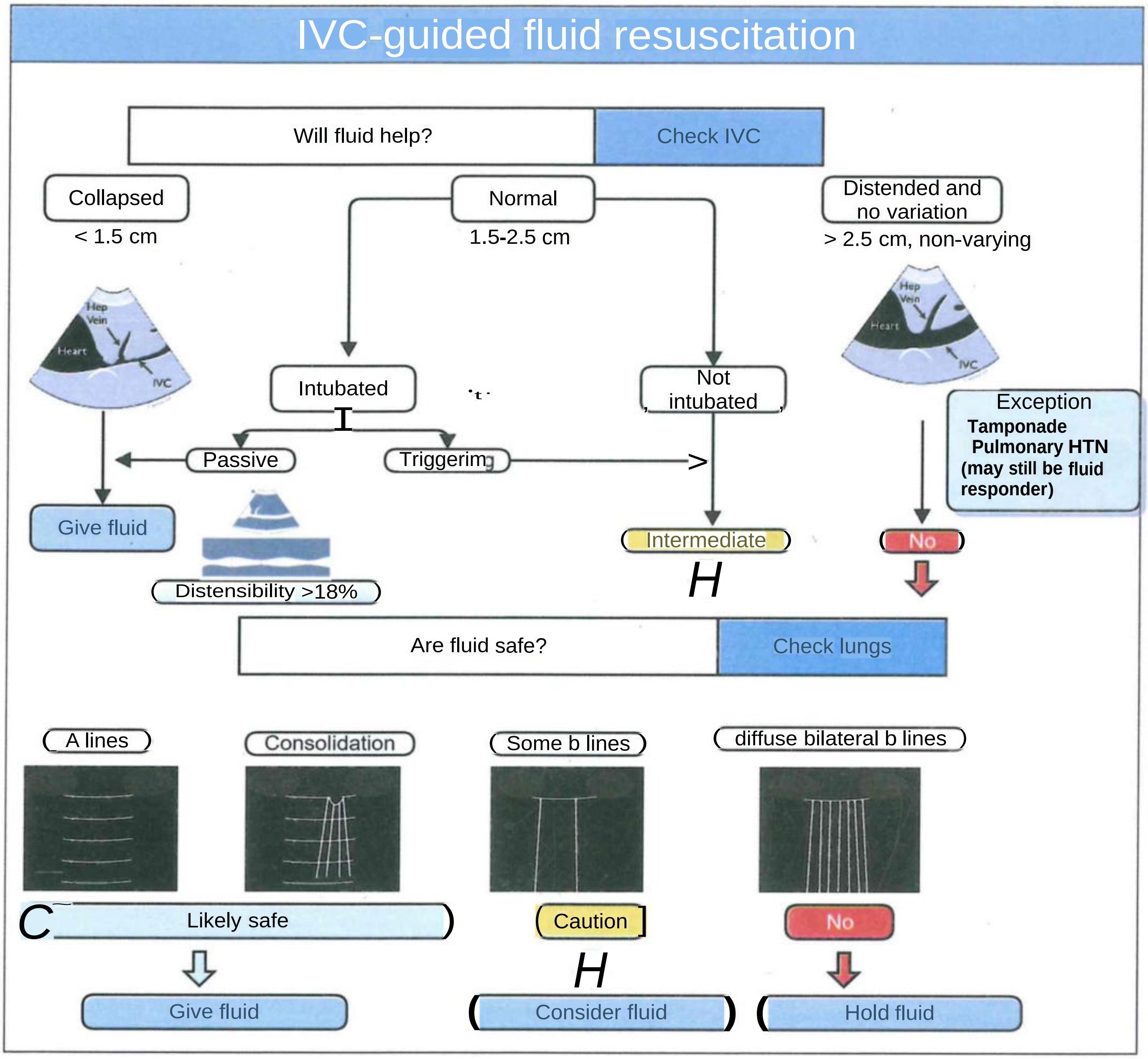

IVC-guided fluid resuscitation
Will fluid help?
Check IVC
Collapsed
< 1.5 cm
Normal
1.5-2.5 cm
Distended and no variation
> 2.5 cm, non-varying
Hep Vein
Heart
IVC
Intubated
Not intubated
Passive
Triggering
Give fluid
Distensibility >18%
Intermediate
Exception
Tamponade
Pulmonary HTN
(may still be fluid responder)
No
Are fluid safe?
Check lungs
A lines
Consolidation
Some b lines
diffuse bilateral b lines
Likely safe
Caution
No
Give fluid
Consider fluid
Hold fluid

Figure 63-3: IVC-guided fluid resuscitation

Focused assessment sonography in trauma (FAST)

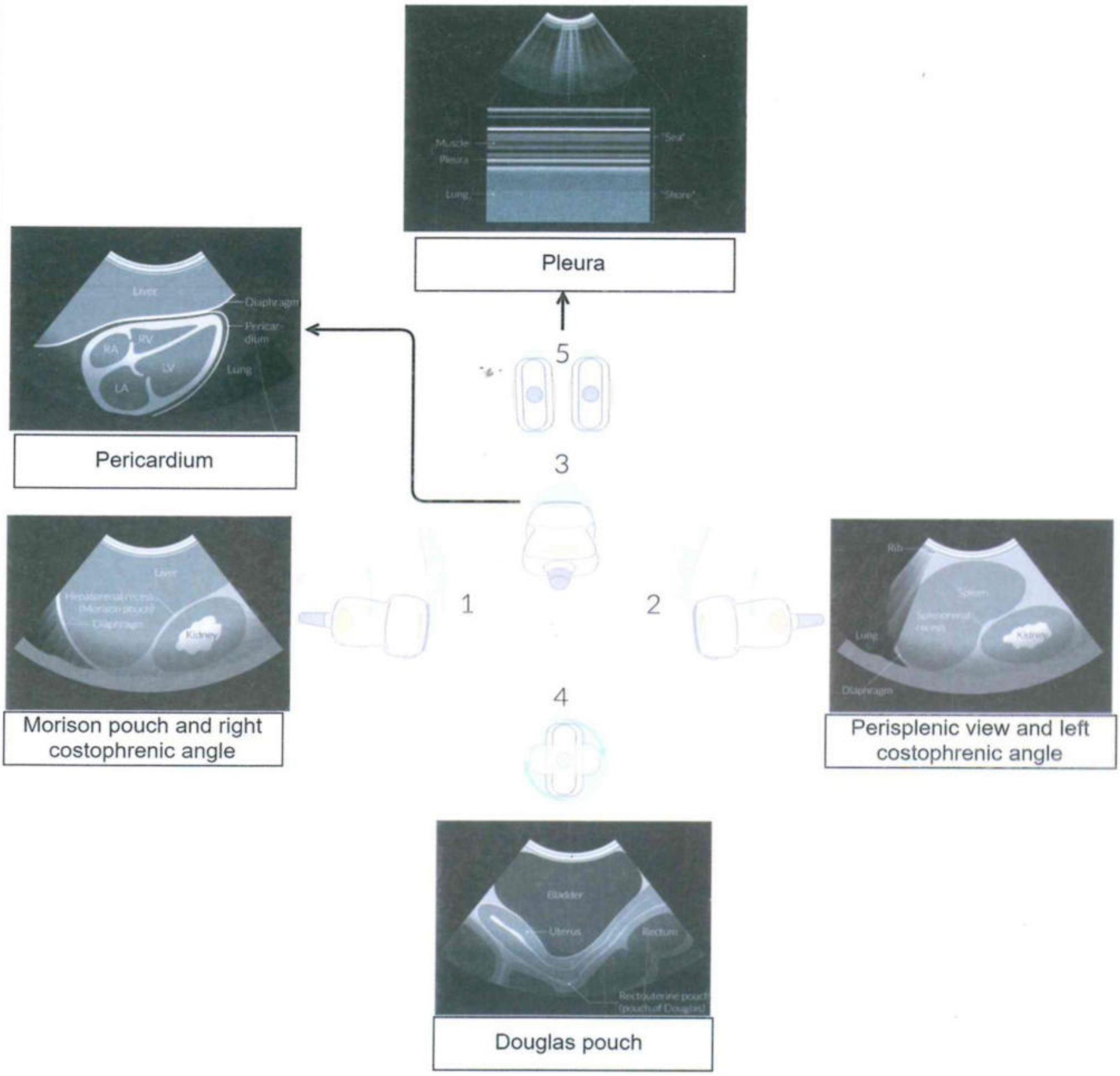

Muscle
Pleura
Lung
"Sea"
"Shore"
Pleura
5
Liver
Diaphragm
Pericardium
RA
RV
LV
LA
Lung
Pericardium
3
Liver
Hepatorenal recess (Morison pouch)
Diaphragm
Kidney
Morison pouch and right costophrenic angle
1
2
Rib
Spleen
Splenorenal recess
Lung
Kidney
Diaphragm
Perisplenic view and left costophrenic angle
4
Bladder
Uterus
Rectum
Rectouterine pouch (pouch of Douglas)
Douglas pouch

Figure 63-5: IVC-guided fluid resuscitation

References

1. Mayo PH, Copetti R, Feller-Kopman D, Mathis G, Maury E, Mongodi S, Mojoli F, Volpicelli G, Zanobetti M. Thoracic ultrasonography: a narrative review. Intensive Care Med. 2019;45:1200–1211
2. Keller M, Magunia H, Rosenberger P, Koeppen M. Echocardiography as a Tool to Assess Cardiac Function in Critical Care–A Review. Diagnostics (Basel). 2023;13:839

anticoagulation
7, 68, 70, 71, 72, 123, 299, 309, 311, 312, 313, 319, 320, 322, 323, 402, 408, 409, 411, 412, 466, 475, 483

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Antiepileptic
195, 490

antifungal
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antimicrobial
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antiplatelet
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